“A CLINICAL COMPARATIVE STUDY BETWEEN BUPIVACAINE WITH CLONIDINE AND BUPIVACAINE ALONE IN PARAVERTEBRAL BLOCK FOR SIMPLE BREAST SURGERY”

A STUDY OF 60 CASES

DISSERTATION SUBMITTED FOR

DOCTOR OF MEDICINE

BRANCH X (ANAESTHESIOLOGY)

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

APRIL 2015

CERTIFICATE BY THE HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"A CLINICAL COMPARATIVE STUDY BETWEEN BUPIVACAINE WITH CLONIDINE AND BUPIVACAINE ALONE IN PARAVERTEBRAL BLOCK FOR SIMPLE BREAST SURGERY"** submitted by **Dr.Y.SUKIRTHARAJ**, in partial fulfillment for the award of the degree of Doctor of Medicine in Anaesthesiology by theTamilnadu Dr.M.G.R. Medical University, Chennai , this is a bonafide original research work done by him in the department of Anaesthesiology and Critical Care,Tirunelveli Medical College, under the guidance and supervision of **Prof.Dr.A.THAVAMANI M.D.,D.A** during the academic year 2012-2015.

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CERTIFICATE BY THE GUIDE

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I, **Dr.Y.SUKIRTHARAJ**, declare that the dissertation has entitled**"A CLINICAL COMPARATIVE STUDY BETWEEN BUPIVACAINE WITH CLONIDINE AND BUPIVACAINE ALONE IN PARAVERTEBRAL BLOCK FOR SIMPLE BREAST SURGERY"**has been prepared by me. This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfilment of the requirement for the award of M.D. Degree, Branch X (ANAESTHESIOLOGY) degree Examination to be held in April 2015.

Place : TIRUNELVELI **DR.Y.SUKIRTHARAJ**

Date :

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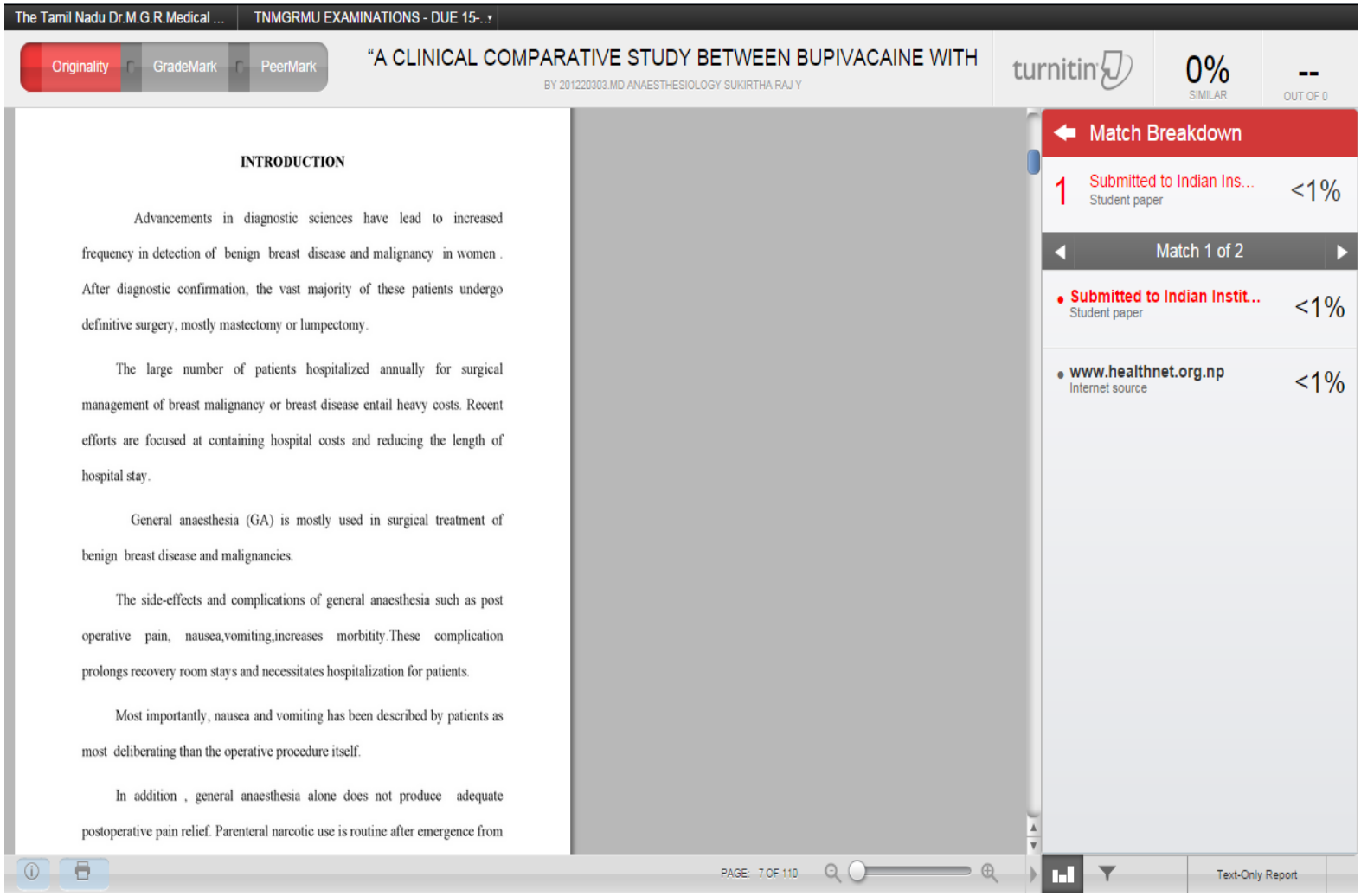
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INTRODUCTION
Advancements in diagnostic sciences have lead to increased frequency in detection of benign breast disease and malignancy in women . After diagnostic confirmation, the vast majority of these patients undergo definitive surgery, mostly mastectomy or lumpectomy.
The large number of patients hospitalized annually for surgical management of breast malignancy or breast disease entail heavy costs. Recent efforts are focused at containing hospital costs and reducing the length of hospital stay.
General anaesthesia (GA) is mostly used in surgical treatment of benign breast disease and malignancies.
The side-effects and complications of general anaesthesia such as post operative pain, nausea,vomiting,increases morbitity.These complication prolongs recovery room stays and necessitates hospitalization for patients.
Most importantly, nausea and vomiting has been described by patients as most deliberating than the operative procedure itself.
In addition , general anaesthesia alone does not produce adequate postoperative pain relief. Parenteral narcotic use is routine after emergence from
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LIST OF ABBREVIATIONS

1.	ASA	American Society of Anaesthesiologists
2.	ATP	Adenosine Triphosphate
3.	COX-2	Cyclooxygenase-2
4.	CPSP	Chronic Postsurgical Pain
5.	CVS	Cardio vascular system
6.	ECG	Electrocardiogram
7.	GA	General Anaesthesia
8.	GABA	γ-aminobutyric acid
9.	HOCM	Hypertrophic obstructive cardiomyopathy
10.	JCAHO	Joint Commission of Accreditation of Health Organisations
11.	MRM	Modified Radical Mastectomy
12.	NIBP	Non Invasive Blood Pressure
13.	NK	Neurokinin
14.	NMDA	N-methyl-d-aspartate
15.	NSAIDS	Non SteroidalAnti inflammatory Drugs
16.	PCA	Patient Controlled Analgesia
17.	PGE2	Prostaglandin E 2
18.	PHN	Postherpetic Neuralgia
19.	PVB	Paravertebral Block
20.	PONV	postoperative nausea and vomiting
21.	SpO2	Peripheral oxygen saturation
22.	SSEP	Somatosensory Evoked Potentials
23.	TPVB	Thoracic Paravertebral Block
24.	TPVS	Thoracic Paravertebral Space
25.	TRPV1	Transient Receptor Potential Vanilloid 1
26.	VATS	Video assisted thoracoscopic surgery
27.	VAS	Visual Analogue Scale

CONTENTS

ABSRACT

Background

General anaesthesia,is currently used anaesthetic technique for surgical treatment of simple breast disease and breast malignancies. Its limitations in the form of poorpostoperative pain control,greater incidence of nausea,vomiting,prolongedrecovery stays andprolonged hospitalizations. Parenteral opioids using inearly postoperative period,it leads to increase incidence of nausea,vomiting and sedation resulting in further prolongation of hospital stay.

Regional anaesthesia using paravertebral block,intercostalblock and epidural anaesthesia has been suggestedas an alternative tecnique in simple breast surgey.Regional techniques reduces postoperative pain leading to decreased requirement of analgesics thereby,indirectly leading to a reduction of postoperative nausea and vomiting(PONV).

This study was planned to assess the efficacy of paravertebral block with bupivacaineand bupivacaine with clonidine used for better surgical anaesthesia and postoperative analgesia in simple breast surgery.

Objectives of the study

- To assess onset of sensory blockade.
- To assess duration of sensory blockade.
- To assess intraoperative&postopeartive hemodynamic response.
- To assess duration of analgesia.
- To study the incidence of complications of paravertebral block.

Materials and Methods

Sixty patients posted for simple breast surgery were allocated into two groups-Group BC (receiving 0.5% bupivacaine with clonidine in PVB) and Group B(receiving 0.5% bupivacaine alone in PVB).Onset of sensory block was assessed using Pinprick test.Duration of sensory block measured .

Level of postoperative pain was assessed using Visual Analogue Scale (VAS).Complication of PVB measured .

RESULTS

Patient with Group BC had faster onset of sensory block ,better intraoperative and postoperative haemodynamic response, prolonged duration of analgesia,when compared with group B.

Both groups had no complications.

Three failure of PVB block in patients of both the groups was recorded.

CONCLUSION

Patients receiving bupivacaine with clonidine and bupivacaine alone in PVB is provides better surgical anaesthesia and prolonged post operative analgesia, improved post operativerecovery,reduced hospital stay,when compared with general anaesthesia.

Keywords

Paravertebral,breastsurgery,sensory block, bupivacaine,clonidine,complication.

INTRODUCTION

Advancements in diagnostic sciences have lead to increased frequency in detection of benign breast disease and malignancy in women . After diagnostic confirmation, the vast majority of these patients undergo definitive surgery, mostly mastectomy or lumpectomy.

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In addition , general anaesthesia alone does not produce adequate postoperative pain relief. Parenteral narcotic use is routine after emergence from anaesthesia and during the early postoperative interval , which further increases

the incidence of nausea, vomiting, sedation and results in prolonged recovery room and stay.

Regional anaesthesia using thoracic paravertebral block (TPVB) is an ideal alternative to general anaesthesia for benign breast disease and malignancies.

Benefits include a reduction in intra operative and postoperative analgesic requirement, prolonged postoperative pain relief,thus improving post operative recovery and indirectly leading to reduced post operative nausea, vomiting and potential for early discharge .

Thoracic paravertebral block involves injection of local anaesthetic at the site of emergence of spinal nerve , from intervertebral foraminae.

The paravertebral space contains dorsal and ventral rami and the sympathetic chain. Hence, infiltration of this space results in unilateral sensory , motor and sympathetic blockade.

Paravertebral block has been used to relieve acute chest wall pain from rib fractures, herpes zoster , pleurisy , to manage acute and chronic post thoracotomy pain , and as an anaesthetic technique for surgery of the chest, breast and cholecystectomy.

Comparing Thoracic epidural anaesthesia with paravertebral blocks in breast surgery, the adverse effects of hypotension and urinary retention are significant problems with epidural analgesia because of bilateral blockade .

Pulmonary function are significantly better in the paravertebral group and stress responses, as measured by cortisol and glucose assay, are suppressed in the paravertebral group, but not in the extradural group .

While comparing intercostal blocks with paravertebral blocks, intercostal block has inherent limitations of inadequate spread at multiple levels, inadequate analgesia and greater rates of complications of pleural or pulmonary damage . Intrapleural analgesia (injection of local anaesthetic between the pleurae) leads to significantly worsened pulmonary function in comparison to paravertebral block.

Paravertebral blocks are relatively easy to learn and perform , have low side effect and no additional nursing surveillance. This leads to early discharge and reduce hospital stay.

Immediatepostoperative analgesia is achieved by preincisional PVB in patients who had undergone breast malignancy surgery.

Paravertebral nerve blocks achieve excellent pain relief and inhibit the neuroendocrine stress response to surgical manipulation.

This study was to assess the efficacy of paravertebral block using clonidine as adjuvant to bupivacaine for surgical anaesthesia and better postoperative analgesia in patients undergoing lumpectomy and simple mastectomy without axillary clearance.

AIM OF STUDY

- To assess onset of sensory blockade by using pinprick test in bupivacaine with clonidine and bupivacaine alone group for breast surgery.
- To assess duration of sensory blockade
- To assess intraoperative&postopeartive hemodynamic response
- To assess duration of analgesia
- To study the incidence of complications of paravertebral block .

REVIEW OF LITERATURE

The history of breast malignancy is a long and far too often tragic one. The earliest recorded cases of the disease date back to ancient Egypt 3500 years ago. The three earliest documented cases arise from the famous Edwin Smith papyrus dating back to 1600 BC. Treatment in those days used to be cauterization of tumours with an instrument known as “the fire drill”.

In 460 BC, Hippocrates , the father of western medicine, described breast cancer as a humoral disease. For him, cancer was caused by the excess of black bile. He named the cancer “karkinos”, a Greek word for crab.

In 200 AD, Galen described a large range of pharmaceuticals agents to treat breast cancer . A number of physicians continued to search for the cause of the disease and an effective remedy . Francois de la BoeSylvius , Jean Astruc, Bernardino Ramazzini, Friedrich Hoffman, Giovanni Morgagni, Johanes de Gorter and Claude Nicholas Le Cat were few prominent among them.

In 1757, Henri LeDran , a French physician , put forward the idea that surgery could actually cure breast cancer as long as the infected axillary lymph nodes were removed .

William Halsted of New York made radical breast surgery the gold standard in the year 1882. Jerome Urban proposed super radical mastectomy in 1949.Alternative forms of surgery were also proposed from time to time as effective surgical remedies of breast cancer- they included prophylactic oophorectomy by George Beatson, adrenalectomy by Charles Huggins and hypophysectomy by Rolf Lefft and Herbert Olivecrona .

Currently different types of treatment are available for patients with breast malignangy. Standard surgical techniques are wide local excision, lumpectomy, segmental mastectomy, total mastectomy,MRM with axillay dissection, radical mastectomy .

General anaesthesia is currently the standard technique used for surgical treatment of breast malignancy. Increasing hospital costs and stay have focused attention on reducing the length of hospital stay for these patients .

Adverse effects and complications of general anaesthesia preclude ambulatory surgery for most patients undergoing breast surgery.

A 59% incidence of nausea and vomiting during the 24-hour interval after breast cancer surgery with general anaesthesia has been reported. This complication prolongs recovery room stays and necessitates hospitalization for patients otherwise able to undergo ambulatory surgery . Most importantly,

nausea and vomiting have been described by patients as more debilitating than the operative procedure itself.

In addition , general anaesthesia alone cannot achieve adequate postoperative pain control. Parenteral narcotic use is routine after emergence from anaesthesia and during the early postoperative period , which further increases the incidence of nausea, vomiting, sedation and results in prolonged recovery and hospital stays.

Regional anaesthesia using paravertebral block is an ideal alternative to general anaesthesia for breast surgery. Benefits include reduction in postoperative nausea,vomiting, pain and potential for early discharge.

Acute pain management came into force as a speciality in 1988 in Seattle where Brain Ready published his concept of acute pain services 27 . Later in 1990 with joint colleges', reported the setting up of acute pain services was recommended at all hospitals.

Pain has been introduced as the fifth vital sign and standards for pain management has been published by Joint Commission on Health Care Organization (JCAHO) in 2001.

HISTORY OF PAIN

Pain derived from Latin word -'Poena' means punishment.

CHARLES BELL and FRANCOIS MAGENDIE demonstrated that dorsal roots of the spinal cord transmit sensory information whereas ventral roots transmit motor information and the idea of specific neural pathway for painful sensations originated.

Alpha 2 agonist have been used by veterinarians for many years for regional analgesia, but is being used in humans since 12 years.

FIG 1 - PAIN PATHWAY

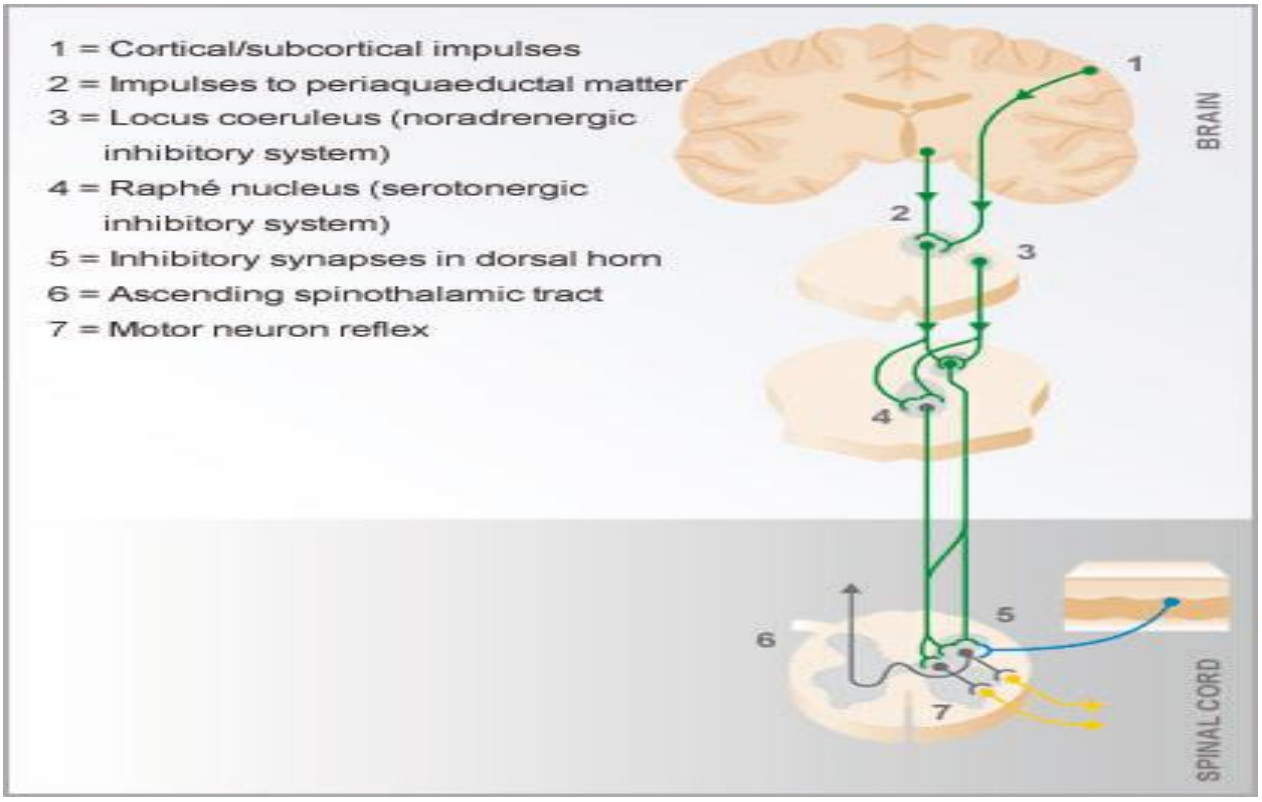
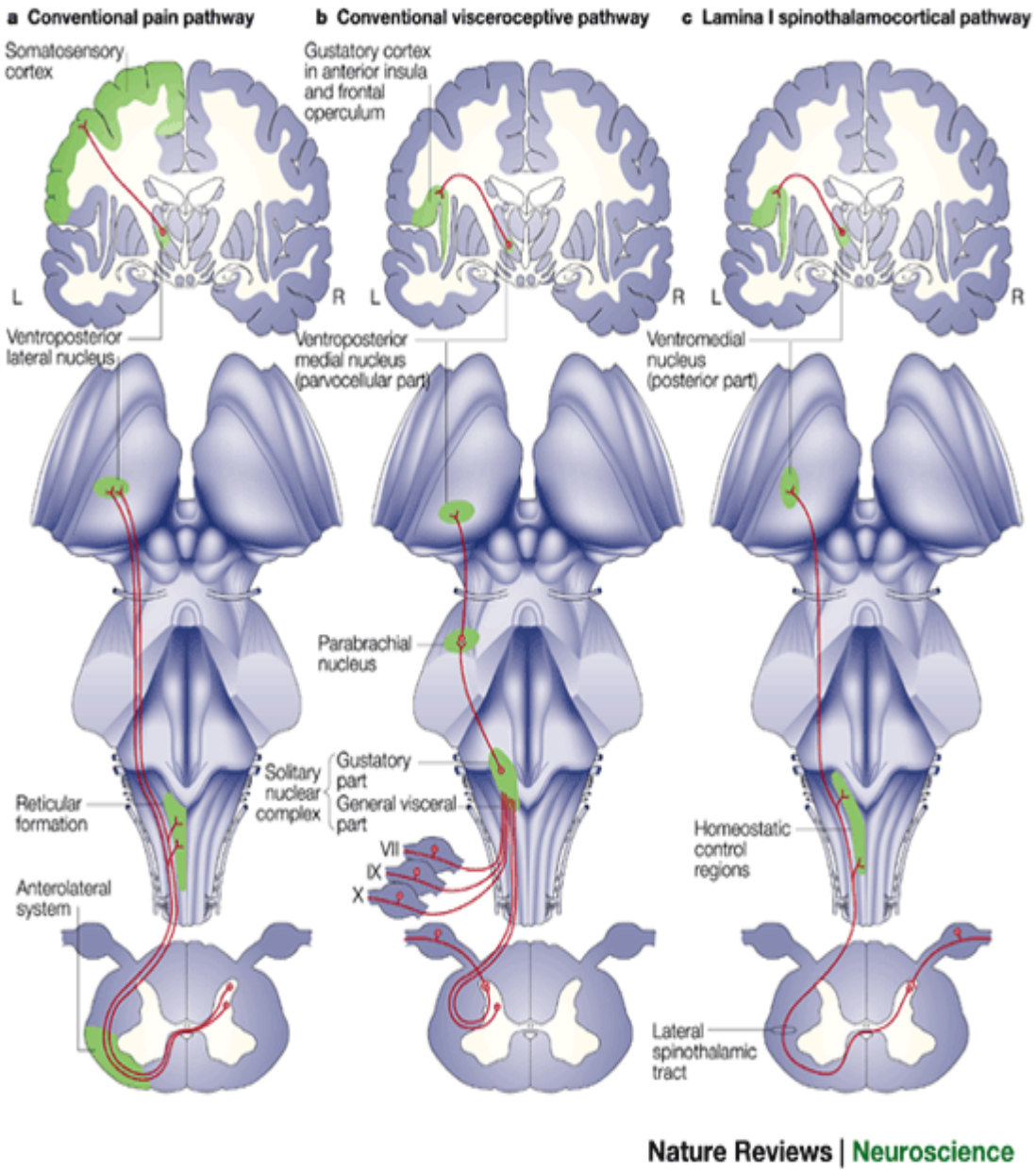


FIG 2 – PAIN PATHWAY



PHYSIOLOGY OF PAIN

Pain is a complex phenomenon which includes sensory –discriminative and motivational – affective components.

The sensory component depends on ascending projection of tracts like spinothalamic and trigeminothalamic tracts into the cerebral cortex. They perceive quality of pain and help to know location of stimulus, intensity and duration of stimulus.

Affective component includes attention, arousal, somatic, autonomic reflex, endocrine and emotional changes

Pain receptors (Nociceptors):

Nociceptors are free nerve endings seen in the skin, muscles, viscera, joints and vasculature. Nociceptors detect the noxious stimulus due to the chemical, mechanical and thermal (heat & cold) changes.

They can be classified into exteroceptors, which receive stimuli from skin surface and interoceptors that are located in the walls of viscera or deeper structures. These are free nerve terminals and are seen adjacent to small blood vessels and mast cells. Nociceptors operate as a functional unit with these.

In addition to nociceptors, somatosensory receptors are located in the skin,which are sensitive to other forms of stimulation and each sensory unit

includes an end-organ receptor, accompanying axon, dorsal root ganglion, and axon terminals in the spinal cord.

In Gate control theory; "Melzack and Wall (1965) proposed that inhibitory interneurons located in the superficial part of the dorsal horn played a crucial role in controlling incoming sensory information before it was transmitted to the brain through ascending pathways".

Dorsal horn contains four major neuronal components:

- The central terminals - primary afferent axons
- Intrinsic neurons
- Projection neurons
- Descending axons that pass caudally from several brain regions.

THE LAMINA OF REXED

"Rexed (1952) divided the dorsal horn of the cat spinal cord into a series of six parallel laminae, based on differences in the size and packing density of neurons (cyto architectonics)".

" Lamina II" can be subdivided into two parts,its inner (IIi) and outer (IIo). Laminae I and II are referred to as the superficial dorsal horn, constitute the main target for nociceptive primary afferents."

The deeper laminae (III - VI) also have an important role in pain. Some nociceptive primary afferents terminate in this region, and many of the neurons

in these laminae including some projection cells are activated by noxious stimulation.

“Lamina I, also called as marginal layer, forms a thin two dimensional sheet covering the dorsal aspect of the dorsal horn and contains both projection neurons and inter neurons”.A few large projection neurons are called as “giant marginal cells of Waldeyer.”

Lamina II is also known as “the substantiagalatinosa, because the lack of myelinatedfibres within it gives it a translucent appearance in unstained sections”.

Lamina III also contains a high density of neurons. Laminae IV - VI are more heterogeneous, with neurons of various sizes, some of which are projection cells.

PRIMARY AFFERENT FIBRES

“The somata of primary sensory neurons that innervate the limbs and trunk are located in sensory gangliaassociated with spinal nerves (dorsal root ganglia). Their axons bifurcate within the ganglion giving rise to peripheral and central branch, where it forms synapses with second-order neurons. Fibres innervating skin are described as cutaneous sensory neurons”.

Afferent fibres innervating abdominal or pelvic viscera are termed visceral afferents.

Cutaneous sensory neurons

- "Myelinated low-threshold mechanoreceptors
- Myelinated nociceptive afferent fibres
- Unmyelinated afferent fibres"

Receptors associated with primary afferent neurons

"Primary afferent fibres also possess a rich diversity of ligand-gated ionotropic, metabotropic and tyrosine kinase receptors which include both the alpha - amino - 3 - hydroxy - 5 - methyl - 4 - isoxazolepropionic acid (AMPA) and N - methyl - D - aspartate (NMDA) classes of ionotropic glutamate receptors and metabotropic glutamate receptors."

Lastly, α_2 adrenergic receptors are also found in sensory neurons and are thought to be localised at the central terminals of peptidergic fibres.

PROJECTION NEURONS, SUBSTANCE P AND THE NEUROKININ 1 RECEPTOR

Neurons with axons that project to the brain are present in large numbers in lamina I and are scattered through the deeper part of the dorsal horn (laminae III - VI) and the ventral horn.

"Lamina I and some of the projection cells in deeper laminae, have axons that cross the midline and ascend to a variety of supra spinal targets including the

thalamus, the midbrain periaqueductal grey matter, lateral para-brachial area of the pons and various parts of the medullary reticular formation."

"Substance P is present in many nociceptive primary afferents and there is evidence that this peptide and the neurokinin I (NKI) receptor, on which it acts, have a significant role in spinal pain mechanisms".

"Substance P is released from primary afferents at extra synaptic sites and acts on NKI receptors on the projection neurons through volume transmission".

SPINAL INTERNEURONS

"Interneurons make up the great majority of the neuronal population throughout the dorsal horn, laminae I - III contains a large number of interneurons since the packing density of neurons is particularly high".

Classification of interneurons inhibitory and excitatory interneurons:

Inhibitory interneurons - divided into those that use GABA but not glycine as transmitters and that use both.

Excitatory interneurons are mostlyglutamatergic.

GABA and GLYCINE receptors:

$GABA_A$and glycine receptors are situated in the spinal cord and are probably expressed by all dorsal horn neurons.

DESCENDING MONOAMINERGIC AXONS:

"Serotoninergic axons in the spinal cord originate in the medullary raphe nuclei, while those that contain norepinephrine are derived from cells in the locus ceruleus and adjacent areas of the pons".

"Norepinephrine containing axons can be identified with antibodies against appropriate synthetic enzymes (eg. dopamine - β hydroxylase). They are found throughout the dorsal horn, with high density in laminae I and II".

Nerve block provide analgesia over the entire area and may have the advantage of blocking the peripheral sensitization. Paravertebral block in breast surgery provides analgesia over the surgical field and by blocking noxious stimuli prevents peripheral sensitization.

THORACIC PARAVERTEBRAL BLOCK

Thoracic paravertebral block was first performed by Hugo Sellheim Leipzig , in obstetric cases (especially LSCS) in 1905,as an alternative technique to neuraxial blockade.

TPVB technique is performing unilateralsympathetic,somatic nerve blockade when local anesthetic agent injectingnear to the spinal nerves along the intervertebral foraminae.Although TPVB have gained a good popularity in 1920- 1930.

It was reintroduced by Eason and Wyatt in 1979.

PVB is used in the following region:

- Cervical
- Thoracic (T1-T10)
- Thoraco-lumbar (T11-L2)
- Psoas compartment (L2-L5)

TPVB technique is performing unilateral sympathetic,somatic nerve blockade when local anesthetic agent injecting near to the spinal nerves along the intervertebral foraminae at unilateral paravertebral space .Two roots of Spinal nerves are dorsal sensory root and ventral motor root.

The dorsal sensory roots are divided into two branches,it passes through the transverse processes.

The ventral motor roots, take the name of intercostal nerves.

ANATOMY OF THORACIC PARAVERTEBRAL SPACE

Its extends from T1 paravertebral space to T12

Thoracic paravertebral space is triangular wedge-shaped.

Superiorly-Costotransverse ligament

Transverse process of vertebrae

Anterolateral parietal pleura

Posteriorly- intercostal membrane and adjacent ribs at superior and inferior.

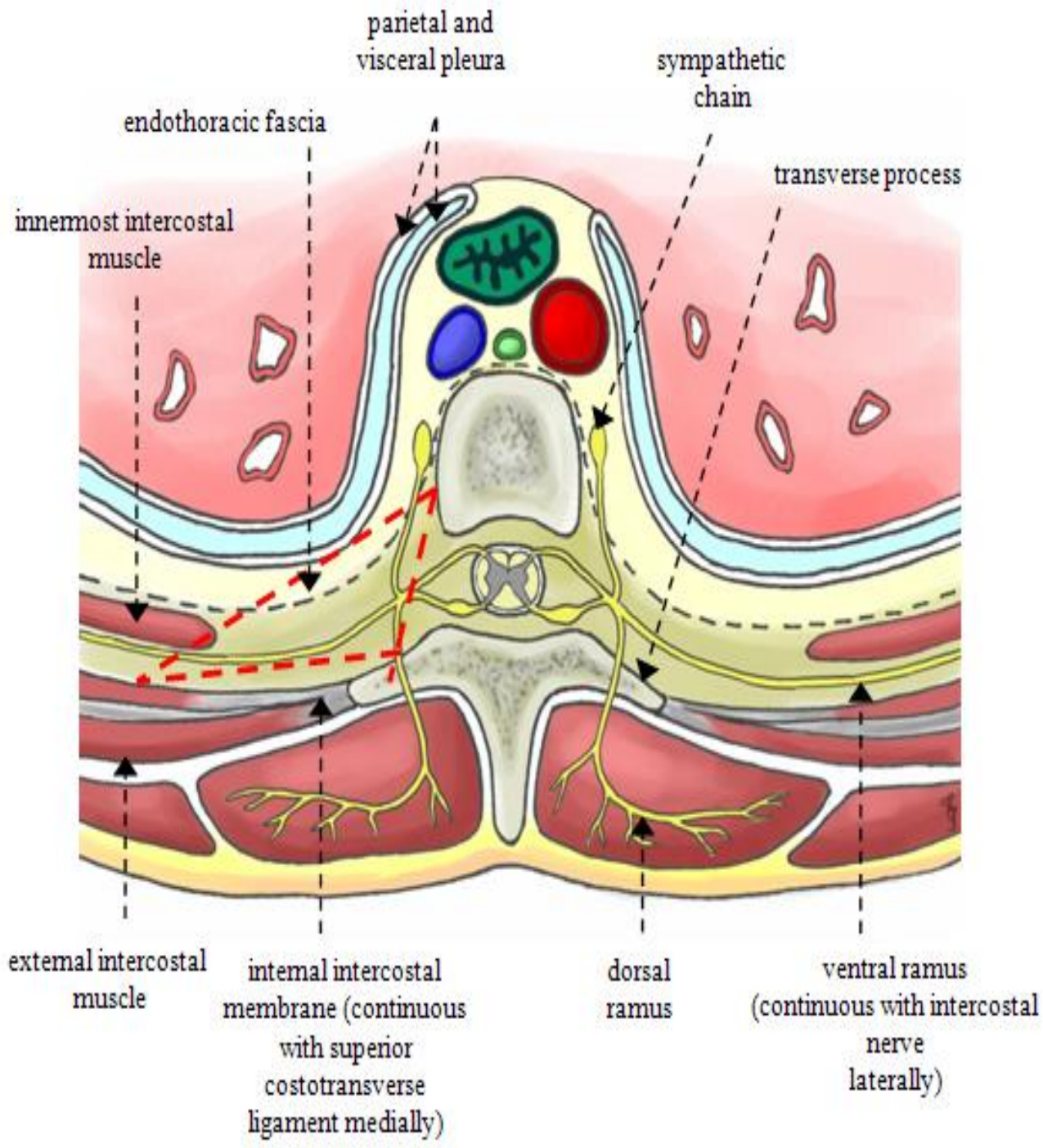
Base of this triangle - Vertebral body,

Intervertebral disc

Intervertebral space at the medial.

Left sided thoracic paravertebral space is larger.

FIG – 3 ANATOMY OF PARAVERTEBRAL SPACE



It is separated into two compartments by Endothoracic fascia.

Anterior compartment- Extrapleural paravertebral compartment

Posterior compartment - Subendotoracic paravertebral compartment .

TPVS communicates medially with the epidural space,Laterally with the intercostal spaces.

Thoracic paravertebral space contains

Adipose tissue,

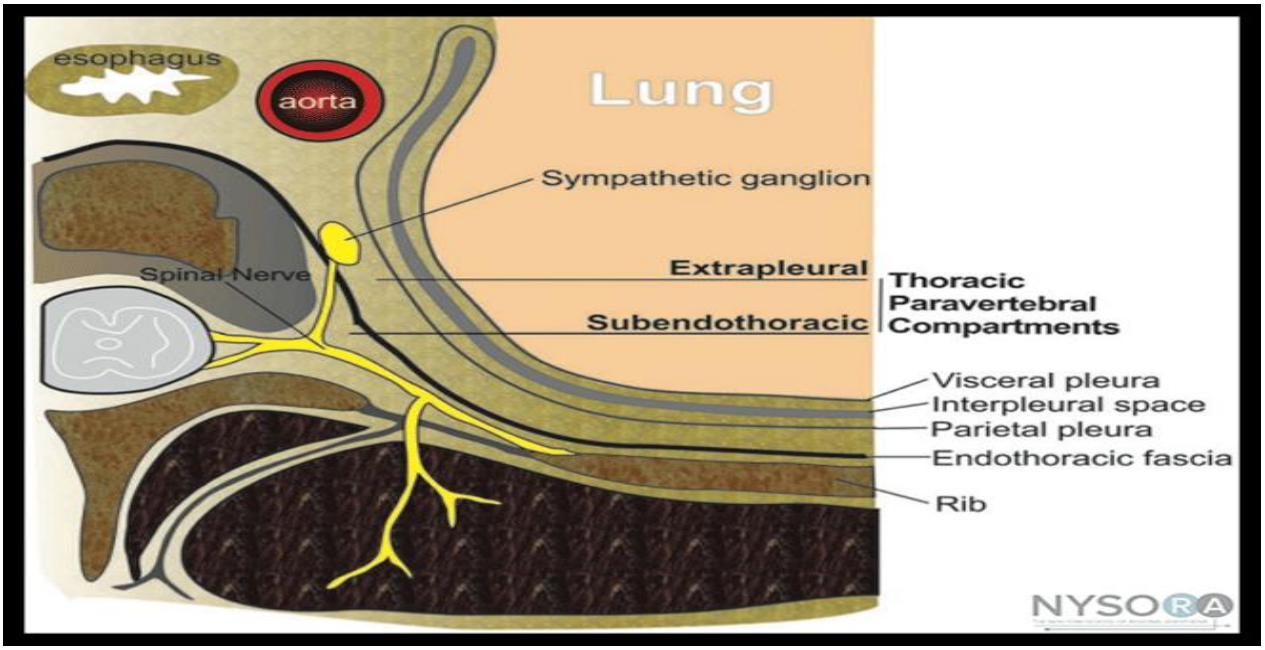
Spinal nerves,

Sympathetic chain,

Intercostal vascular structures,

Preganglionic white and postganglionic grey rami communicantes.

FIG - 4 COMPARTMENT OF PARAVERTEBRAL SPACE



INDICATIONS

Thoracic paravertebral block is used for surgical anaesthesia and postoperative analgesia.

Primary indications as surgical anaesthesia

- Simple breast disease excision, lumpectomy, mastectomy with axillarydissection,MRM.
- Breast reconstruction and reduction surgery
- Resections of chest wall disaese
- Video-assisted thoracoscopic surgery (VATS)
- Upper extremity orthopaedic surgery
- Endovascular aortic aneurysm surgery

Post operative pain control

- In Thoracotomy.
- Minimally invasive cardiac surgery
- Cardiac surgeries including sternotomy , thoracotomy
- Thoracoscopy
- Flial chest
- Inguinal hernioplasty
- Lap or open cholecystectomy

- Post nephrectomy
- Postherpetic neuralgia(PHN)
- Infectious and neoplastic syndromes
- Post mastectomy pain
- Chronic postthoracotomy pain

CONTRAINDICATIONS

Absolute contraindication

- Patient refusal
- Infection at insertion site
- Unspecified neuropathy
- Allergy to local anesthetics
- Major coagulopathy

Relative contraindication for TPVB

- Coagulopathy
- Bleeding disorders
- Anticoagulants applied and kyphoscoliosis.

POSITION AND LANDMARKS

TPVB techniques performing following position of the patient

Sitting

Lateral decubitus

Prone position.

Landmarks

“The spinous process of thoracic vertebrae are angled caudally such that the superior aspect of the tip of the spinous process lies adjacent to the transverse process of lower vertebrae . It means, tip of the spinous process of T1 is adjacent to the transverse process of T2”.

“ For example if T2-T6 are to be blocked, a mid line between the superior level of theT1 and T5 spinous process is marked. The superior aspect of each spine is then marked along the line. A parasagittal line, parallel and 2.5cm lateral to the midline mark is drawn on the side to be blocked. A transverse process lies deep to each parasagittal mark”.

In sitting position,head and neck are at flexion .Anasthesiologist stands behind the patient . The conventional loss of resistance technique is used .

The spinal processes of vertebras are marked with palpation at the level of T1-T6 dermatomes.

The points of needle insertions, at a vertical plane parallel to midline at 2-2.5 cm are also marked lateral to spinous process.

Parts were cleaned and painted with antiseptic solution.

Sterile drapes were placed.

Planned needle insertion point was infiltrated with local anaesthetic.

Tuohy's epidural needle is perpendicularly inserted from skin to hitch transverse process at 3-5 cm depth.Syringe which is prefilled with air is connected to the Tuohy's epidural needle.

After hitching the tranverse process ,needle is superiorly walked off and on advancement of needle for 0.5to1cm,a loss of resistance to air could be elicited.

Syringe was detached from needle and drug was injected in.

In single level block total volume of drug injected was 21 ml

In multiple level block amount of drug injected was 3-4 ml/dermatome.

At time of injection , negative aspiration was done to prevent intravascular injection.

Maximum dosage used was 3 mg/kg of body weight.

Patient was then made to lie down supine.

Onset of sensory anaesthesia occured 10 -15 minutes after the injection.

Table-1VARIOUS PARAVERTEBRAL BLOCK TECHNIQUES

S.NO	PARAVERTEBRAL BLOCK TECHNIQUES
1	Blind technique
2	Loss of resistance technique
3	Nervestimulation techniques
4	Ultrasound guided technique
5	Pressure monitoring technique
6	Fluoroscopic directly imaging technique
7	Direct application technique at the time of thoracoscopy or thoracotomy or surgical placement

DOSAGE AND SPREAD

In multiple level injection ,the amount of localanesthetic agent needed for each dermatomes is 4 – 5 ml of 0.5% bupivacaine, 0.5% levobupivacaine, 2% lidocaine.

For single level paravertebral block, 0.5% bupivacaine or 0.5%levo bupivacaine 20-24 mL of local anesthetic used.

The spread of drug in paravertebral space is usually cephalad and then caudal.

“ Cloud” spread in few segments,lateral spread to intercostal space and medial spread to epidural space may occur.

In epidural injections; cephalic3-4 dermatomes and caudally 2-3 dermatomes spread are seen.

But,in paravertebral block; cephalic2-3 dermatomes and caudal 3-4 dermatomes spread are seen.

In our study,both the techniques of multiple and single level injection were used.

If multiple level injected, the amount of localanesthetic agent has to be calculated as 3-5 ml (0.5% bupivacaine with clonidine (2mics/kg) or 0.5% bupivacanine alone) for each segment of respectivegroup.

For single injection technique, 20-21 ml local anesthetic(0.5% bupivacaine with clonidine(2mics/kg) or 0.5% bupivacanine alone) for complete block.

Table 2 - Local anaesthetics used for PVB with typical onset, anaesthesia and analgesia times.

Local Anaesthetic	**Onset time(min)**	**Anaesthesia time / hours**	**Analgesia time / hours**
Bupivacaine 0.5%	15-25	4-6	12-18
Ropivacaine 0.75%	10-15	4-6	12-18
Lidocaine 2%	10-15	2-3	3-4
Mepivacaine 1.5%	10-20	2-3	3-4

COMPLICATIONS OF PARAVERTEBRAL BLOCK

- "Failure of "PVB" (6.8 to 10%)
- Pneumothorax .
- Bradycardia
- Hypotension , because of unilateral sympathetic blockade.
- Accidentally intravascular injection of local anaesthetic toxicitiy has ocurred.
- When needle is introduced medially, dural puncture ocurred. This lead to Epidural spread or epidural anaesthesia, spinal anesthesia and postdural headache .
- Unilateral Horner's syndrome is due to spread of local anesthetic to ipsilateral stellate ganglion or preganglionic fibers.
- Unilateral sensory block in arms is due to spread of local anesthetic to T1 segment of brachial plexus".

CLINICAL ADVANTAGES

- "Learn easily and perform PVB
- Better than thoracic epidural administration
- Complications are less in PVB
- In single level injection, developed unilateral somatic and sympathetic block in many dermatomes
- Decreased stress and pressor response to surgical stimulae.

- Hemodynamic stability is better than GA
- Lower extremity motor function is present
- Bladder sensation is present
- Early mobilization is possible
- Less hospital stay".

PHARMACOLOGY OF BUPIVACAINE

Bupivacaine is an amide type local analgesic drug.

It is a hydrochloride salt of 1-butyl-N-(2, 6-dimethylphenyl) piperidine-2-carboxamide.

It was synthesized in Sweden by Ekenstam and his colleagues in 1957.

First used clinically by L.J. Telivuo in 1963.

Pka is 8.2

Molecular weight	-	288
Protein binding	-	95%
Lipid solubility	-	28
Elimination half life	-	210mts
Toxic plasma concentration	-	>1.5µg/ml
Approximate duration of action	-	175mts

The drug is very stable to acids, alkalis and repeated autoclaving.

Bupivacaine 0.5% is the preferred strength.

Higher concentration result in greater variability of spread.

Bupivacaine is 4 times as potent as lignocaine, hence 0.5 % solution is approximately equivalent to 2 % lignocine.

It is more cardiotoxic than lignocaine which is aggravated by hypoxia, hypercapnia and pregnancy.It causes more sensory than motor block .

It is not recommended for intravenous regional analgesia.

Duration of effect is between 5 and 16 hours and is one of the longest acting local analgesics, which is related to binding of it to the nerve tissue.

Small percentage of a given dose of drug is excreted unchanged in the urine and the remainder is metabolised in the liver.

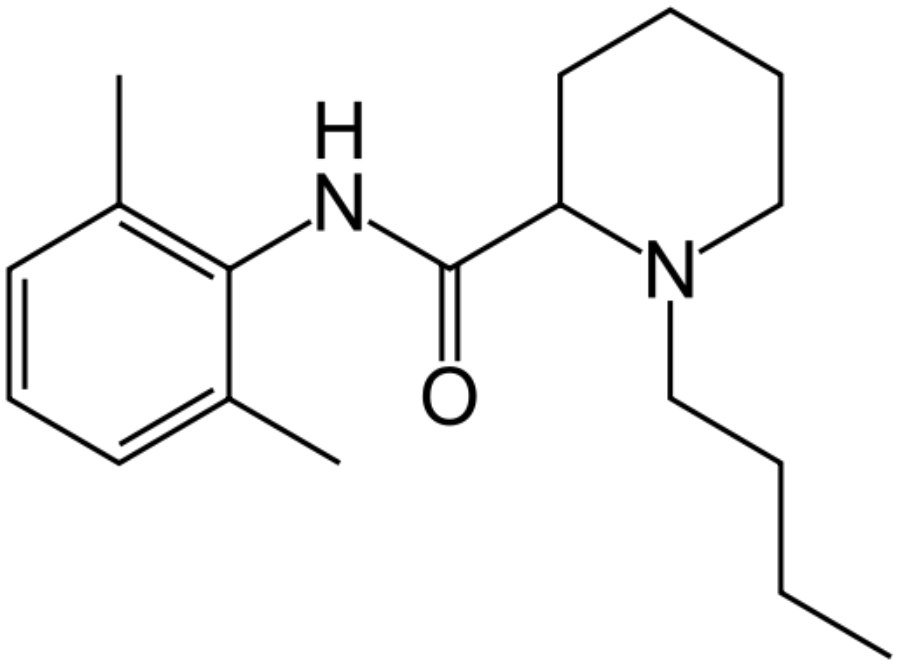
Uses:

- Spinal anesthesia
- Epidural anesthesia
- Caudal anesthesia
- Continuous epidural anesthesia
- Peripheral nerve block
- Infiltration anesthesia

Onset Time and Duration of Action

Site of action	Onset (minutes)	Duration (minutes)
Intrathecal	5	90-120
Epidural	15-20	165-225
Brachial plexus	10-20	600

FIG -5 STRUCTURE OF BUPIVACAINE



Pharmacokinetics

It gets absorbed through nerve rootlets and it is rapidly absorbed from the site of injection, but the rate of absorption depends on the vascularity and the presence of vasoconstrictors.

Because of high lipid solubility it easily penetrates nerve and vascular tissue.

80-95% of absorbed bupivacaine binds to the plasma proteins.

Distribution:

Rapid distribution phase: (α)

Slow disappearance phase: (β)

Biotransformation:

Possible pathways of metabolism of bupivacaine include aromatic hydroxylation and conjugation.

Only the N-dealkylated metabolite, N-desbutyl bupivacaine has been measured in blood (or) urine after epidural (or) spinal anesthesia.

Alpha1 acid glycoprotein is the most important plasma protein binding site of bupivacaine.

The concentration of bupivacaine is increased in many situations such as post operative trauma.

Excretion:

It is through the kidney, 4-10% of the drug is excreted unchanged.

Mode of Action

a)Site of action

i) The spinal nerve rootlet fine nerve filaments having a large surface area are exposed to local anesthesics.

ii) Posterior and lateral aspects of spinal cord.

b)Sodium Channel blockade:

They impede sodium ion access to the axon interior by occluding the transmembrane sodium channels thus delaying the process of depolarization and axon remains polarized. It is a non-depolarisation blockade. Thus the resting membrane potential is maintained and depolarization in response to stimulation is inhibited.

The mechanism by which local anasthetics block sodium channel conductance is as follows,

- Local anesthetics in the cationic form act on the receptors within the sodium channels, on the cell membrane and block it. The local anaesthetic can reach the sodium channel either via the lipophilic pathway directly across the lpid membrane or via the axoplasmic opening.This mechanism accounts for 90% of the nerve blocking effects of amide local anaesthetics.
- The second mechanism of action is by membrane expansion .This is a non specific action in contrast to the more specific drug receptor interaction.

Pharmacodynamics:

It has got a longer duration of action but a slower onset.

Cardiovascular system:

It reduces cardiac output by reducing the sympathetic tone, by slowing the heart rate and by reducing the venous return.

It produces a fall in arterial blood pressure but it is relatively slow and is seldom very profound.

It produces a fall in central venous pressure.

It causes an increase in lower limb blood flow.

It causes a reduction in incidence of deep vein thrombosis.

Respiratory System

It relaxes bronchial smooth muscle. It causes apnea due to phrenic and intercostal nerve paralysis or depression of the medullary respiratory center following direct exposure to drug.

Gastro intestinal tract:

There is an increase in gastro intestinal motility and emptying of the gastric contents are better.

Toxicity:

Toxicity is related to plasma level of unbound drug and more likely due to an inadvertant intravenous injection.

Systemic toxicity reactions primarily involve central nervous system and cardio vascular system.

The blood level required to produce central nervous system toxicity is less than that required to produce circulatory collapse.

Central Nervous System Toxicity:

"Early symptoms are circumoral numbness, tongue paresthesia and dizziness. Sensory complaints include tinnitus and blurred vision.

Excitatory signs (restlessness, agitation, nervousness, paranoia) often precede central nervous system depression (slurred speech, drowsiness, unconsciousness)".

Muscle twitching heralds the onset of tonic clonic seizures.

Respiratory arrest often follows.

The excitatory reactions are the result of selective blockade of inhibitory pathways.

Cardiovascular System Toxicity:

The rate of depolarization in fast conducting tissue of purkinje fibres and ventricular muscle is decreased.

The rate of recovery of bupivacaine induced block is slower than that of lignocaine.

Extremely high concentration of the drug causes sinus bradycardia, hypotension, AV block, idioventricular rhythms, and life threatening arrhythmias such as ventricular tachycardia, ventricular fibrillation and cardiac arrest.

TREATMENT OF BUPIVACAINE TOXICITY

CNS toxicity

Convulsions treated by adequate ventilation with oxygenation, and controlled by anticonvulsantdrugs.Diazepam (10–20 mg IV, repeatedif necessary) or Alternatively, thiopental (150–250 mgintravenously) can be used. Treatment includes mechanicalventilation and circulatory support, and the use of a vasopressor may be indicated.

CVS toxicity

If ventricular tachycardia, ventricular fibrillation and cardiac arrest occurred then , Bretylium is drug of choice.Phenytoin and Amiodarone are also used.

Bupivacaine is highly protein binding and highly tissue binding mainly to cardiac tissue hence it will be unable to revive the patient even after effective resuscitation with adrenaline and vasopressin.

Usage of 20% lipid emulsion will reduce the toxicity of bupivacaine by binding to it.

Dosage and preparation

The dosage of bupivacaine depends on,

- Area to be anaesthetized
- The vascularity of the tissue to be blocked
- The number of neuronal segments to be blocked
- Individual tolerance
- Technique of local anesthesia

Available concentrations

0.25%,0.5%

0.25%,0.5% soluble in isotonic saline

0.5% 0.75% solution in 8% dextrose hyperbaric

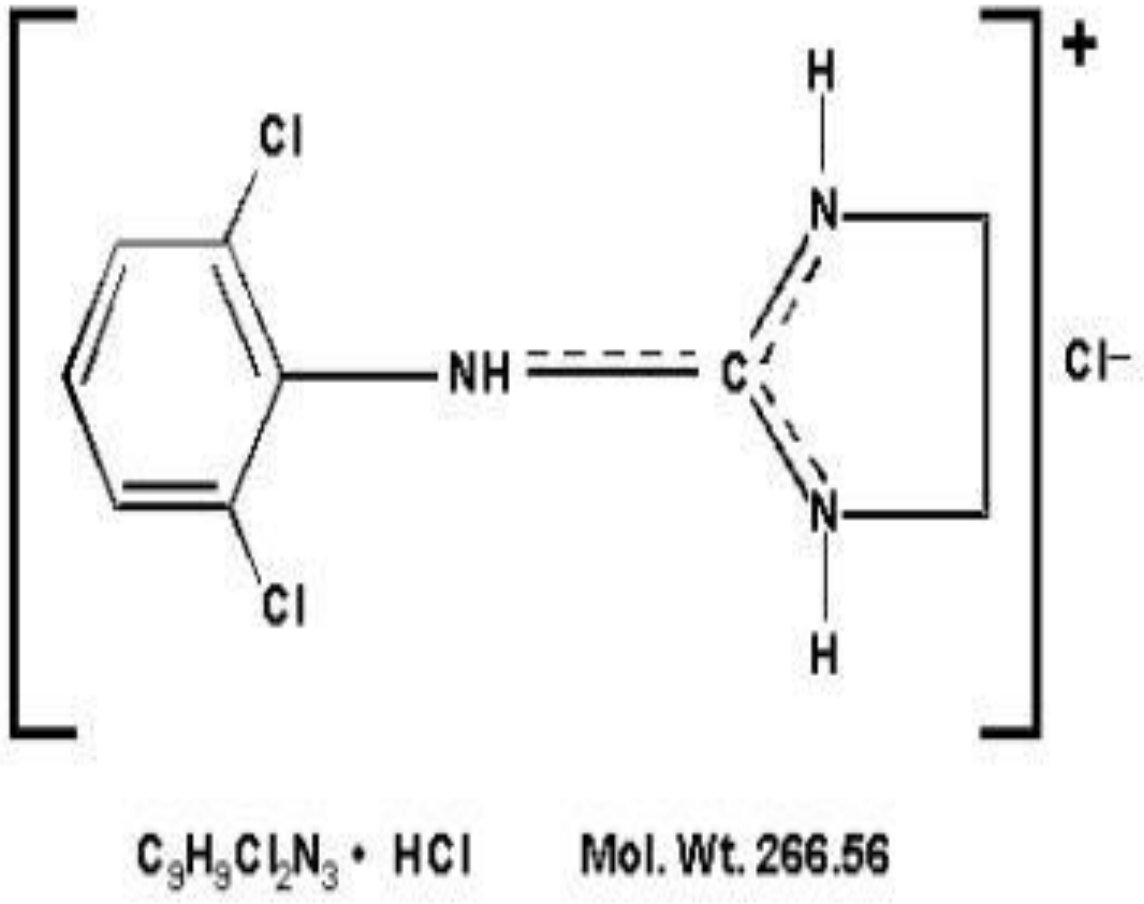
These doses can be repeated in 3-4 hours but maximum dose is 400mg in 24 hours.

Table:3 Dosage and concentration of bupivacaine in various blocks

Type of block	concentration	Dosage in ml	Dosage in mg
Local infiltration	0.25-0.5%	5-20ml	Upto 75 mg
Brachial plexus block	0.25-0.5%	20-40ml	75-225 mg
Intercostals block	0.25-0.5%	3-5ml	15-20mg per each nerve
Epidural block	0.25-0.5%	15-20ml	50-225mg
Caudal block	0.25-0.5%	15-30ml	75-150mg
Subaracnoid block	0.5%	2-4 ml	10-20mg
Paravertebral block	0.25-0.5%	15-20ml	50-225mg

CLONIDINE

FIG 6 –STRUCTURE OF CLONIDINE



$C_9H_9Cl_2N_3 \cdot HCl$ Mol. Wt. 266.56

History and chemistry

Clonidine hydrochloride, an imidazoline derivative was introduced as a nasal decongestant and vasoconstrictor.

This drug is related to the drug called naphazoline, still this has complex profile of actions.Its hypotensive and bradycardia effects were first appreciated in 1962.

It is a centrally acting adrenergic agonist that lowers blood pressure by decreasing basal sympathetic system activity.

It was introduced in Europe in1966 and subsequently in the U.S as an antihypertensive agent.(220:1 alpha2:alpha1)

2-(2,6_-dichlorophenylamino)-2 – imidazoline hydrochloride.;

C9H9C12N3 Hcl.

Molecular weight :266.56

It is an odourless ,white, bitter crystalline substance soluble in alcohol and water.

Mechanism of action

Alpha-2 adrenergic agonists produce clinical effects by binding to alpha -2 receptors .

Three subtypes of alpha 2 receptors;

- Alpha 2a- sedation,analgesia,sympatholysis.
- Alpha2b-vasoconstrction (antishivering mechanism)
- Alpha 2c- startle response

It is response of body and mind to unexpected stimulus, such asloud noise, flash light. Effects are centrally mediated by partial adrenergic agonist (alpha2:alpha1=200:1). The site for sedation is the pontine locus ceruleus of brain stem, where as principal site of analgesia is most likely spinalcord.

FIG 7- PHYSIOLOGY OF ALPHA-2 RECEPTORS

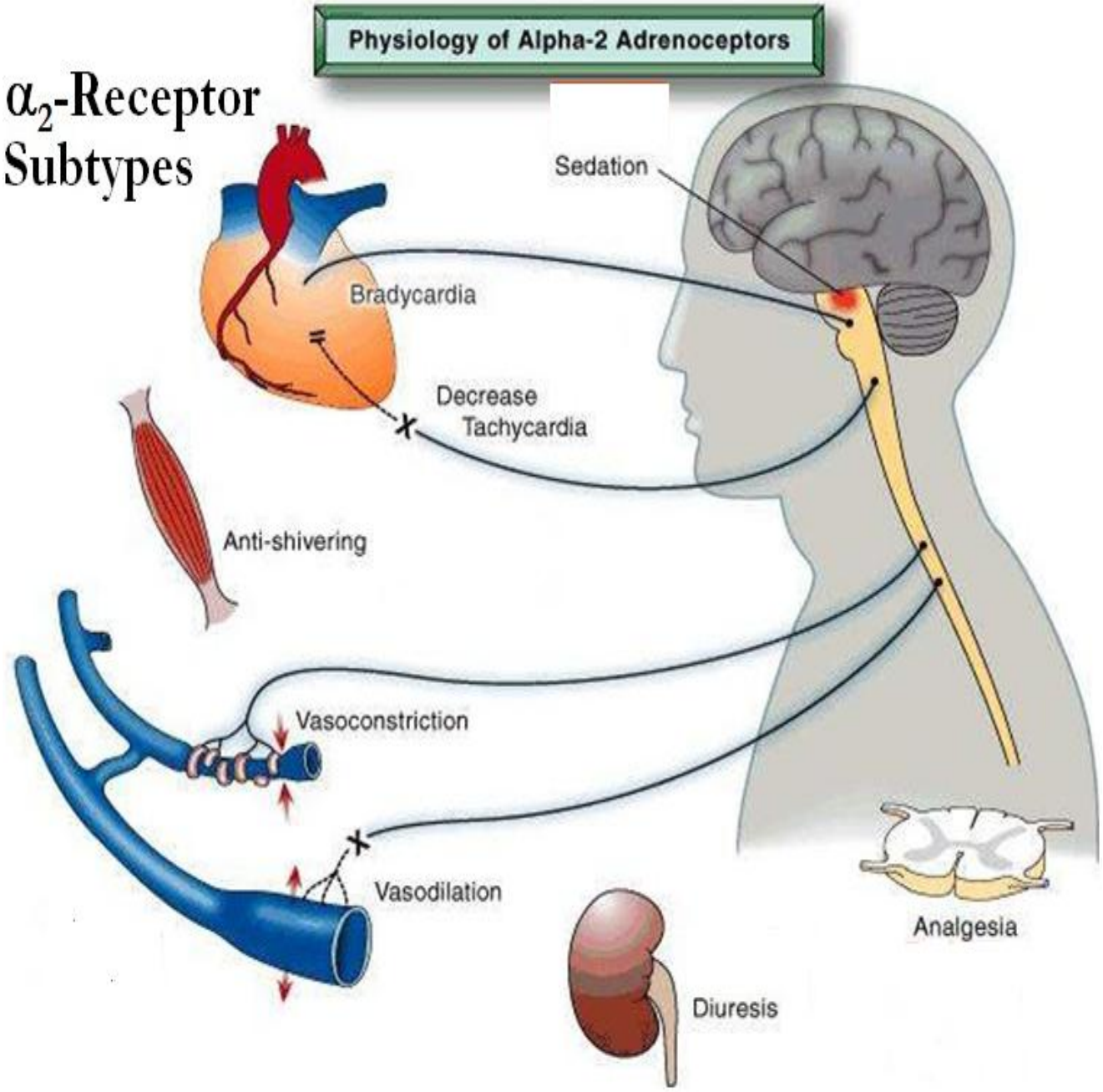
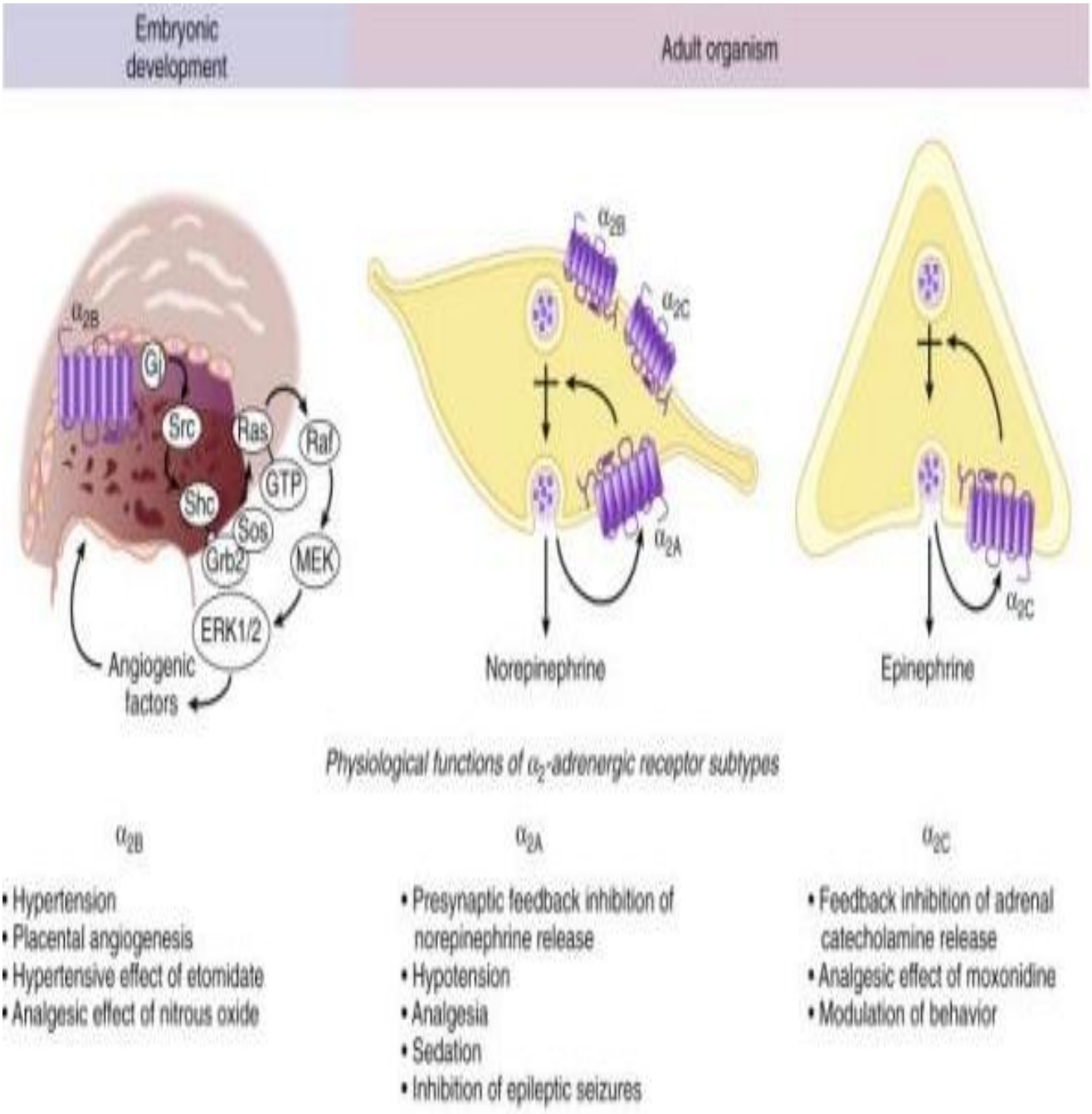


FIG 8 – ACTION OF ALPHA-2 RECEPTORS



In the CNS, their main sites of action include the tractus solitarius (leading to hypotension and bradycardia),the locus coeruleus (causing sedation) and certain vagal nuclei.

In addition, they have profound analgesic effects.These may involve actions at spinal and supraspinal sites, including enhancement of descending inhibitorypathways to the dorsal horn, as well as the depression of thalamocortical pathways.

Their peripheral effects decrease heart rate and reduce vascular smooth muscle tone.This leads to peripheral vasodilatation and bradycardia,hypotension,reduced cardiac output.

Clonidine has the ability to modify potassium channels in CNS and leads to hyperpolarisation of the membranes hence it reduces anaesthetic requirements. Clonidine inhibits release of substance P and Sand neuron firing produced by the noxious stimulation. This leads to analgesic effect.

Clonidine also reduces the cold response threshold by synchronous acting, while leading to mild elevation of the sweating threshold.It acts on the central thermoregulatory system rather than preventing shivering peripherally.

Pharmacological effects

Intravenous administration of clonidine produces a transient rise in blood pressure associated with peripheral vasoconstriction, an effect which is mediated by alpha1-adrenoceptors. However, the secondary responses of bradycardia and hypotension are mainly due to agonist effects on alpha2 adrenoceptors in the CNS.

Pharmacokinetics

Clonidine is rapidly absorbed after oral intake and has 100% bioavailablity.

It attains peak plasma concentration within 60 to 90 minutes

The elimination half life is around 9-12 hours.

50% metabolized in the liver, 50% excreted in an unchanged form by the kidney.

Its half life is increased in renal failure and liver failure.

Transdermal delivery system is available in which the drug is released at a constant rate for about a week. Steady state concentrations will be achieved in three to four days.

Side effects;

Sedation and xerostomia is most common

Fatigue,weakness,headache,withdrawal syndrome

Pallor ,weakly positive coombs test

Fever may also rarely occur.

CVS orthostatic symptoms,palpitation,tachycardia,bradycardia,conduction abnormalities (i.e,junctional bradycardia,High degree Atrioventricular block and sinus node arrest)CCF and raynauds phenomenon syncope.

CNS

Nervousness, mental depression,insomnia,agitation may occur.

Other behavioral changes , vivid dreams or nightmares, hallucinations and delirium are rarely reported.

Dermatological

Rash, pruritis,angioneuroticedema and urticaria,alopecia.

Gastrointestinal

Nausea, vomiting,anorexia,malaise,abnormalities in LFT ,constipation,abdominal pain rarely.

Genitourinary

Decreased sexual activity,impotence.

Hematological

Reduced platelet count rarely.

Metabolic

Weight gain,gynaecomastia, transient hyperglycemia , increased serum CPK

Musculoskeletal

Myalgia,arthralgia,leg cramps.

INTERACTIONS WITH VARIOUS OTHER PHARMACOLOGICAL PREPARATIONS

This drug may also like other ones are seen to be reacting with other different drugs namely:

- Tricyclic anti-depressant drug
- Chlorpromazine.

Because of these specific interactions, the intended anti-hypertensive nature of the drug may be very much reduced and affected.

Clonidine may cause bradycadia or AV block hence to be used in patients on digitalis,CCB,beta blockers with a caution.

Toxicology

Some of the studies supported the occurence of spontaneous retinal degeneration in albino rats treated with clonidine for more than six months.

In some studies conducted in dogs and monkeys clonidine showed a high drug concentration in choroid ,but in human studies they documented dryness of eyes only Electroretinography macular dazzle retinal function was normal.

Over dosage

Hypertension followed by fall in BP,HR,respiratory rate, temperature, altered consciousness,decreased or absent reflexes,seizures,weakness and miosis.

Reversibe cardiac conduction abnormality,apnea,coma may occur.

Toxic effects are developed within 30 minutes to two hours after exposure.

In paediatric patients,even a small dose of 0.1mg clonidine may produce toxic effects.

Antidote

There is no specific antidote for clonidine .

Now adverse clinical effects can be reversed by ATIPAMAEZOLE(specific antagonist)in recently ingested patients.

Gastric lavage ,activated charcoal may be useful.

Supportive care may include anticholinergic for bradycardia , IVF and vasopressors for hypotension and vasodilators for hypertension.

Table - 4 Available formulation of clonidine

Formulations	Brand	Dosage
Oral tablets	Clonidine tablets	0.1,0.2,0.3mg
Transdermal patch	Clonidine TTS	0.1,0.2,0.3g 3mg/day
Combination tablets	Clonidine and chlorthalidone	0.1,0.2 or 0.3 mg clonidine+15mg chlorthalidone
Injection	Cloneon , duraclon	500,150,100mcg/ml

Table - 5 Various routes of clonidine

Route	Dose
Intranasal	2-4mcg/kg
Intramuscular	2mcg/kg
Oral	4-5mcg/kg
Rectal	2.5-5mcg/kg with atropine 40mcg/kg
Intravenous	1-2mcg/kg bolus or 0.18-3.16 mcg/kg/hrinfusion
Caudal anaesthetic adjuvant	1-2mcg/kg
Spinal anesthetic adjuvant	1-2mcg/kg
Epidural anesthetic adjuvant	0.0625%bupivacaine with fentanyl 1mcg/ml and clonidine 0.6 mcg/ml
Sciatic block	0.2% ropivacaine 0.4mg/kg/hr with clonidine 0.12 mcg/kg/hr infusion

Anaesthetic uses of clonidine

The anesthetic use of an alpha 2 adrenergic receptor agonist has been of recent research interest over last 20 years.

1.Premedication

It can be used as premedication.

Clonidine's sedative effect is by activation of involved in sleep wake cycle.

In addition it also has an anaesthesia sparing effect.

It reduces the dose of intravenous hypnotic drugs and MAC of volatile anaesthetic agents.

Clonidine has been recommended in doses of 4mcg/kg intranasally or orally and rectally in a dose of 5micg/kg causes adequate sedation.

Routine use of anticholinergic with clondine reduces the incidence of bradycardia and hypotension.

Its use as a premedicant is more useful in certain group of patients like,

- Drug addicts and alcoholics,most of these patients have withdrawal symptoms and sympathetic system activity is high, when compared to normal patients.
- Patients on chronic opioid or analgesic treatment for cancer pain.These patients have increased analgesic requirement intraoperatively..
- Hypertensive patients.

2. Control of hemodynamic response

Hemodynamic effects of clondineare both central and peripheral.

Stimulation of the peripheral sub endothelial receptor causes vasoconstriction transiently.

Stimulaton of alpha 2 adrenergic receptors of the neurons in the nucleus tractus solitaries causes inhibiton of nucleus of sympathetic neurons in the medulla,and reduces the baroreflex activity,decreases the atrial pressure hence leads to fall in heart rate.

It is interesting to note that phasic activity of this reflex is preserved.Hence any decrease in arterial pressure is followed by a significant increase in heart rate.

It depress presynaptic sympathetic neurons at thoracic spinal cord level (lateral horn).

Vasoconstrictors (eg.phenylephrine) and anticholinergics are used to treat the hypotension and bradycardia.

Clonidine prevent stress response due to laryngoscopy, intubation, extubation and surgical stimulation .

Patients undergoing cardiac surgery and vascular surgery have superior control of hemodynamics ,reduce the incidence of myocardial ischemia and decrease the morbidty and mortality.

3 Post operative analgesia and regional anesthesia:

It inhibit transmission of nociceptive stimuli in the dorsal horn of the spinal cord..clonidine has additive effect with opioids and augment local anesthetic blockade and prolong duration.

Epidural:

It can be used as whole anaesthetic agent to produce epidural analgesia in large doses (upto2-300mcg/day).

At these dose hypotension ,bradycardia are common.

It is more commonly used along with local anesthetics and opioids at a dose of 10-15 mcg/hr.

Spinal:

Compared to morphine intrathecal clonidine produces analgesia of shorter duration but without respiratory depression or urinary retention,along with local anesthetics 1-2mcg/kg can be given.

Caudal:

Clonidine prolongs duration of block without hemodynamic alterations. The recommended dose is 1-2mcg/kg.

Labor analgesia:

Epidural clonidine can be used alone or with opioids or local anesthetics .

Clonidine crosses the placenta but not affect the newborn.

The recommended dose is 100mcg during labor.

Peripheral nerve blockade:

Clonidine reduces the failure rate, and reduces local anesthetic dose requirement, prolonging sensory blockade and duration of post operative analgesia.

A small dose of 2-3mcg/kg is sufficient which obviously reduce the risks of side effects.

The quality of Bier's block (IVRA) by clonidine with lignocaine is improved. Addition of 150mcg clonidine has been found to enhance the tolerance.

Other uses are

- Prevention of emergence agitaton.
- Decreasing minimum alveolar concentration of sevoflurane.
- Postoperative nausea and vomiting (PONV).
- Hypotensive anesthesia
- In cardiovascular surgery; better hemodynamic stability in patients posted for cardiac surgery.
- Prevent intraoperative shivering as well as post operative.
- Day care surgery;

REVIEW OF LITERATURE

Darren Koh Liang Khai et al, studied, using the single level-injection thoracic paravertebralblock of ropivacaine 1% to provide analgesia in breast surgery in Asian patients in the Singapore General hospital and documented 32 cases scheduled for elective MRMwith axillary dissection. All patients received 20 ml ropivacaine 1% with adrenaline (5 ug/ml) injected into the paravertebral space before surgery. Also all patient recieving GA with conventional regimen. They Observed peri-operative

analgesic requirement,pain score, shoulder movement limitation, nausea or vomiting, and adverse effects of the block.

In another study**, HuraG Knapiket al**,seventy patients to received 0.5%ropivacaine and 0.5% bupivacaine inPVB for MRM, onset of sensory block and duration of sensory blockade was analysed in both the group similar level of analgsia achieved.

GROUP	ONSET OF SENSORY BLOCKAE WITH IN 5 MIN	TOTAL DURATION OF SENSORY BLOCKADE > 24 HRS
R	53%	81%
B	20%	50%

C. L. Burlacu ,H. P. Frizelle et al, study observed, fentanyl and clonidine in combination with diluted levobupivacaine (0.05%) in PVB are effective analgesic, lead to decreased requirement of morphine consumption post operatively.Low dose of fentanyl or clonidine in PVB was not associated any side-effects. 0.1% Levobupivacainealone in PVB is ineffective for postoperative analgesia after breast surgery.

Sang ii park et al, Non-obstetrical surgery is harmful to both the mother and the fetus,during first trimester. Anaesthetist also at stress , as the anaesthetic agents are harmful to fetus . A case of breast abscess at 8 weeks pregnancy was successfully

treated by thoracic paravertebral block without any complications and provided with adequate post operative analgesia. Thoracic paravertebral block is safe anesthetic technique for non-obstetric surgery during early pregnancy.

Pusch et al. described a singleinjection of a high volume of bupivacaine into the thoracic paravertebral space and reported effective anaesthesia for breast lump excisions as well as mastectomies with axillary dissection.

In a study conducted by **Pekka et al**, a PVB with bupivacaine (1.5mg/kg) at T3, performed before general anaesthesia in patients scheduled for modified radical mastectomy(MRM), resulted in less need for postoperative opioid analgesics in the first hours after sur gery and in less overall intensity of pain on the first postoperative day. The fact that the initial postoperative analgesia was relatively good may have had certain beneficial consequences. For instance, the smaller amount of opioid consumed by the PVB patients in comparison with control patients, was probably an explanation for the rapid psychomotor recovery and infrequent postoperative nausea and vomiting in the patients given PVB with bupivacaine before surgery.

Rising hospital costs have focused attention on the length of stay for patients undergoing surgical treatment of breast cancer. Thus far, ambulatory surgery has been limited by side-effects and complications of general anaesthesia. Paravertebral block offers the potential of effective analgesia, with limited postoperative nausea and vomiting. In a retrospective study involving fifteen

patients with breast cancer who underwent sixteen major operations for the treatment of breast cancer using paravertebral block**, Weltz et al** proved that paravertebral block achieved effective anaesthesia for cancer operations of the breast and axilla. Sensory block persisted for an average of 23 hours and postoperative pain was effectively controlled. In nine patients were discharged home after an average recovery room stay of 169 mintues. All patients who underwent planned admission for postoperative observation were discharged by the morning after operation and one patient was discharged within four hours of operation

In a retrospective analysis of 145 consecutive patients undergoing breast cancer operations using paravertebral block and 100 patients undergoing general anaesthesia during a 2-year period performed by **Coveney et al**, surgery was successfully completed in 85% of the cases attempted by using paravertebral block alone and in 5.7% of the cases surgery was completed by using paravertebral block supplemented with local anaesthetic . PVB block resulted in a significantly shorter hospital stay than general anaesthesia for all operations. Forty four of the patients undergoing PVB (28.2%) were discharged on the day of surgery compared to 11% of the patients undergoing GA. In total, 3.8% of patients receiving PVB remained in the hospital for more than twenty four hours compared with 24% of patients undergoing GA.Narcotic analgesia was required in 98% of general anaesthesia patients as opposed to 25% of patients undergoing paravertebral block. Twenty percent of patients in the paravertebral group required medication for nausea and vomiting during their hospital stay compared with 39% in the general anaesthesia group.

Cosmetic and reconstructive breast augmentation is a frequently performed surgical procedure-especially in those women undergoing modified radical mastectomy for breast cancer.In a prospective,single blinded randomized trial by **Klein et al**, paravertebral block was found to provide improved analgesia during the first 24 hours after breast surgery when compared with GA ,along with lower nausea and vomiting scores which may in part be the result of improved analgesia and reduced intake of postoperative opioids.

In another prospective ,randomized ,double blinded ,placebo controlled study comprising of eighty eight patients scheduled to undergo elective mastectomy, **Moller et al** deduced that the group receiving multilevel paravertebral block prior to general anaesthesia required less intravenous fentanyl for intraoperative and postoperative analgesia in comparison to the group receiving only general anaesthesia.A multilevel injection PVB was shown to produce a more reliable sensory block than a single injection technique. Single injection techniques of paravertebral block are limited by the duration of action of the local anaesthetic. Recent improvements in the needle design and the introduction of disposable infusion pumps have facilitated the use of ambulatory perineural infusions after extremity surgery.

Buckenmaier et al described two case studies where both patients of breast cancer who underwent major breast surgeries were administered paravertebral block and an epidural catheter with an attached disposable infusion pump was secured .Infusion

was started at the end of surgery and continued for one additional postoperative day. Patients were discharged from hospital with clear instructions regarding local anaesthetic toxicity,pump function and catheter removal. Both the cases showed satisfaction with the anaesthetic technique.

D'Ercole and associates,in a case report , have mentioned use of PVB in a pregnant patient requiring modified radical mastectomy with axillary dissection. A 38 yr old primigravida at 29 weeks of gestation presented with infiltrating ductal carcinoma grade 3 that required urgent left MRM. PVB was performed at T1-6 level and surgery was performed under sedation with intravenous propofol infusion .Both the intraoperative and the postoperative periods were uneventful.

Good immediate postoperative analgesia is achieved by providing preincisional PVB in patients undergoing breast surgery for cancer. Good acute pain relief is associated with a lower risk of development of chronic pain in the operative area.

Pekka et al, a prospective, randomized ,placebo-controlled, single blinded study involving sixty breast cancer patients undergoing breast surgery, administered PVB to one group before general anaesthesia and surgery, while the other group received a placebo block followed by general anaesthesia and surgery. A one year follow up was done postoperatively. Their follow-up showed that preoperative PVB reduced the prevalence and severity of pain upto one year after breast cancer surgery. Diagnostic and minor therapeutic breast surgery is usually performed in an outpatient setting.

The anaesthetic technique should aim at fast recovery and adequate postoperative pain relief. This cannot always be achieved with general anaesthesia which may be associated with considerable postoperative pain and a frequent incidence of postoperative nausea and vomiting. PVB seems to be a solution for these problems.

In a prospective study conducted by **Terheggen et al**, thirty patients scheduled for elective, outpatient, minor breast surgery were randomized into two groups to receive either PVB or GA. Pain scores were significantly lower in the PVB group. The patient satisfaction score was significantly higher in the PVB group.

Another similar study was conducted by **Cooter** and associates , where a total of 100 patients undergoing submuscular breast augmentation were administered paravertebral blocks. This prospective study showed that 87% of the blocks were successful for surgical anaesthesia and 94% of the blocks were successful for postoperative analgesia. The pain scores were also significantly less, therby, suggesting PVB as a safe and effective anaesthetic technique for such minor surgeries.

In a study conducted by **Ebrahimy M & Moradi AR** for postoperative survey for the effective duration of the paravertebral block with bupivacaine in patients planned for mastectomy operations,the average duration of analgesia was seventeen hours and all the patients were pain free for the first eight hours after surgery. All the patients expressed their satisfaction with the procedure.

Hypertrophic obstructive cardiomyopathy (HOCM) places patients at significant risk of sudden cardiac death along with other cardiac disorders especially when placed under surgical stress. They can present with significant management difficulties. **Buckenmaier and colleagues** reported use of paravertebral block in a patient of HOCM who presented for partial mastectomy with axillary lymph node dissection. Compared to general anaesthesia PVB provides profound, long lasting sensory deafferentation. The resulting greater attenuation of the surgical stress response may translate into reduced iontropic stimulation of the heart.In comparison to the regional anaesthetic techniques

such as spinal or epidural anaesthesia which produce bilateral sympathectomy resulting in profound hypotension ,difficult to treat in HOCM patients, PVB induced hypotension is a rare phenomenon

In a study conducted by **Greengrass et al**,twenty five patients undergoing breast surgery were provided paravertebral block with sedation as an alternative to general anaesthesia .Postoperatively , patients had minimal nausea , vomiting and pain and the procedure was satisfactory for all patients.

Buckenmaier and colleagues , in a study involving twenty patients undergoing mastectomy or breast lumpectomy with axillary dissection, used paravertebral block with infusions of 0.2% ropivacaine at 10 ml/hr. Infusions were continued for the patients during their home stay. Patients were contacted daily and again after one week following catheter removal and queried on visual analog pain scores (VAS) and narcotic use. All the patients were pleased with their pain control. This technique

achieved profound chest wall analgesia that extended beyond 24 hrs while still preserving the ambulatory status of the patients.

Thoracoscopic surgery can be associated with considerable postoperative pain . In a study conducted by **Vogt and colleagues**, forty patients planned for thoracoscopic surgeries were selected and divided randomly into two groups –one group receiving paravertebral block along with i.v. patient controlled analgesia (PCA) with morphine while other group was treated with a placebo block and morphine PCA. Paravertebral block improved postoperative pain treatment after thoracoscopic surgery in a clinically significant fashion.

Neurological assessment after thoracic aortic aneurysm repair is important for detecting and treating late onset paraplegia .Traditional methods of pain control, such as patient – controlled intravenous analgesia and epidural analgesia, may interfere with neurological assessment. In a case study conducted by **Shine and colleagues**, a patient who had a repair of thoracoabdominal aneurysm received continuous thoracic paravertebral analgesia that provided excellent analgesia while preserving the ability to monitor neurological function. In addition, it facilitated early extubation and maintainance of normal blood pressure with minimal use of adjuvant vasoactive medications. Analgesic methods that allow restitution of spontaneous ventilation improve venous return from vessels emanating from the spinal cord ,thus enhancing one aspect of spinal cord protection protection. Central neuraxial analgesia almost invariably affects hemodynamics, usually as a consequence of a significant

sympatholytic effect on capacitance vessels.The volumes of local anaesthetic required to maintain central neuraxial analgesia may also increase pressure within the central neuraxis, with possible detrimental effects on cord perfusion in pathologic circumstances.

Thoracic epidural analgesia may also affect the cardioaccelaratory fibres.It may also be contraindicated in the setting of thoracic abdominal aortic aneurysm repair because the large dose anticoagulation used in these procedures may increase the occurrence of central neuraxial hematoma. In contrast to both central neuraxial analgesia and systemic opioids, paravertebral analgesia provides intensive unilateral analgesia with infrequent neurological and hemodynamic effects.

Paravertebral blockade has been used for minimally invasive cardiac operations to facilitate early tracheal extubation. After minimally invasive coronary artery bypass procedures, paravertebral block is as effective as thoracic epidural blockade, with fewer side effects .When used for postthoracotomy analgesia, paravertebral blockades result in better preservation of pulmonary function than epidural analgesia.

In a letter to the editor, **Toshiyuki Saito** has mentioned of a case study where a single injection paravertebral block has produced multisegmental analgesia The study involved 16 normal healthy human volunteers, in whom 22 ml of 1% lidocaine was administered at T 11 level in the paravertebral region. Analgesia, heart rate, blood pressure and body temperature were monitored. Volunteers were administered with control injection of paravertebral saline. Right sided analgesia was induced with

lidocaine in all subjects in contrast to no block with saline. Analgesia developed in a mean of 12 dermatomes with sympathetic blockade in at least 6 dermatomes. The cardiovascular response was no change in blood pressure or heart rate. There were no side effects or complications. Paravertebral block has been found to cause improvement in coronary perfusion.

In a case study conducted by **Ho and colleagues**, resolution of ST segment depressions after right thoracic paravertebral block during general anaesthesia was reported and attributed mainly to the paravertebral block- induced sympathectomy. The fact that ST segment depression resolved after the thoracic paravertebral block suggests that the block may have direct stenotic coronary artery dilating effects.

The treatment of postherpetic neuralgia (PHN) continues to be a challenge in clinical pain management. In a case study involving one hundred thirty two patients with acute herpes zoster, **Genlin Ji and coworkers** assessed the effectiveness of repetitive paravertebral injections with local anaesthetics and steroids for the prevention of postherpetic neuralgia. The incidence of PHN was significantly lower in the paravertebral group .

In a case report, **Borene and colleagues** mentioned about a 51 yr old woman who developed severe lymphoedema and brachial plexopathy following modified radical mastectomy and radiotherapy for breast carcinoma. A continuous cervical paravertebral block was performed with good analgesic effects.The VAS score was never reported to be >2 after surgery and no systemic analgesics were required throughout the postoperative period 85.

In a case study by **Meguiar and colleagues**, bilateral lumbar paravertebral block was given to forty primigravidas during stage I of labour Good analgesia was obtained while maternal mean blood pressure and pulse were unchanged without any compromise of fetal well being and labour progressed rapidly.

Thoracotomy induces severe postoperative pain and impairment of pulmonary function. Risk of pulmonary complications may be reduced by adequate analgesia and physical therapy . Since acute postoperative pain is also a predictor of long term pain after thoracotomy, early and aggressive treatment of pain may help to reduce high frequency of chronic pain . Although thoracic epidural analgesia is commonly considered the gold standard for postoperative pain treatment after thoracotomy,this technique may fail, be contraindicated or not be possible for a variety of reasons. Evidence has suggested that paravertebral block is also an effective technique for analgesia in thoracotomy, which is associated with fewer side effects than epidural analgesia.In a systematic review of randomized trials, **Joshi and associates** compared epidural versus paravertebral and other alternative regional analgesic techniques for postoperative pain,analgesic use and complications. Paravertebral block was found to have comparable analgesic effects with fewer side effects in comparison to epidural technique.

MATERIALS AND METHODS

Source of Data

The study was conducted in Tirunelveli Medical College Hospital, a tertiary care hospital. Hospital Ethical Committee approval was obtained. Patients scheduled to undergo elective surgery like lump excision, simple mastectomy, wide local excision, Webster procedure for gynaecomatia under TPVB with clonidine,as adjuvant to bupivacaine were enrolled in this study.

This was a Prospective, randomized, comparative ,observer blinded study

Inclusion criteria

1. Adult patients aged between 18-60 yrs.

2. ASA I ,ASA II physical status.

3. Diagnosed cases of simple breast disease.

4. Patients scheduled for elective surgery like

- Lump excision
- Simple mastectomy
- Wide local excision
- Webster procedure for gynaecomatia

Exclusion criteria

- Patient refusal
- Bleeding disorders.
- Allergy to amide-type local anaesthetics.
- Infection at injection site.
- Pregnant patient
- Breast feeding females.
- Severe obesity (BMI>35 kg/ m 2).
- Psychiatric disorders.
- Patients with past history of musculoskeletal disorders.
- Additional surgical procedure during the same surgical time.
- Previous history of thoracic or abdominal surgeries.

SAMPLE SIZE

GROUP BC(n-30) - received 21 ml of 0.5% bupivacaine with clonidine (2 mics/kg) in Thoracic paravertebral block.

GROUP B (n-30) - received 21ml of 0.5% bupivacaine with 1ml of isotonic normal saline in thoracic paravertebral block.

RANDOMISATION

Sixty consecutive adult patients were studied.

Informed Written consent was obtained from all patients.

The study population was randomized via sealed envelopes technique allocated into two groups as under-

GROUP BC was taken as bupivacaine +clonidine group

GROUP B was taken as bupivacaine group.

PRE OPERATIVE EVALUATION

In all the patients,

- Age
- I.P. No
- Body weight and
- Baseline vital parameters were recorded.

History regarding Previous anaesthesia, surgery, Any significant medical illness,Medications and Allergies were recorded.

Complete physical examination and airway assessment were done.

Following laboratory investigations were done

- Haemoglobin %,
- Blood sugar & urea
- Serumcreatinine
- Urine analysis.
- Bleeding time and clotting time

METHOD

On the day of surgery, for patients coming to theatre, intravenous access was obtained using a 16 G or 18 G intravenous canula, 5mL/kg/h infusion of Ringer Lactate fluid was started.

All patients were premedicated with midazolam 2mg iv and fentanyl 50 mics iv before performing block.

HR, MAP and SpO2 were recorded before and after performing block.

Technique:

Monitoring: NIBP, ECG, SpO 2.

Patient position: Sitting, Rt or Lt lateral decubitous

FIGURE - 9 Equipments

Equipments

22 G short bevelled Tuohy's epidural needle

20 ml syringes (2 in nos)

5 ml syringe with 1 ½ " 25 gauge needle for skin infiltration

Local anaesthetic agents- 0.5% Bupivacaine & 2% Lignocaine

Clonidine ampoule

Sterile towels and gauze packs

Sterile gloves

Marking pen

Antiseptic solution for cleaning and painting of part

Normal saline

FIGURE – 10 Needle Insertion Point

Needle Insertion Point:

In breast surgery involved dermatomes T1-T6, 2-2.5 cm lateral to tip of spinous process of corresponding T1-T6 vertebrae .

FIGURE – 11 Performing TPVB

PROCEDURE

Part was cleaned and painted with antiseptic solution.Sterile drapes were placed. Planned needle insertion point was infiltrated with local anaesthetic. Tuohy's epidural needle perpendicularly inserted from skin to hinge transverse process at 3-5 cm depth. Syringe with prefilled air was connected to the Tuohy's epidural needle

From the tranverse process,needle is superiorly walked off, and advanced 0.5 to 1cm.On introduction loss of resistance to air could be elicited.

Syringe was detached from the needle and drug injected.In single level technique total volume of drug 21 ml was injected or in multiple level block 3-4 ml of drug/dermatome was injected. At the time of injection , negative aspiration was done to prevent intravascular injection.

Maximum dosage used was 3 mg/kg of body weight. Patient was then made to lie down supine .Onset of sensory anaesthesia occured 10 -15 minutes after the injection.

Group BC was injected with 21 ml of 0.5% bupivacaine with clonidine (2 mics/kg).

Group B was injected with 21 ml of 0.5% bupivacaine with 1ml of normal saline.

After the block patient was sedated with intravenous opioids.

Oxgenation with facemask (4lit/min).

In case of any block failure, patient excluded from the study.

Onset of Sensory block,HR, MAP, and SpO2 were recorded 5, 10,15,20, 30, 45,60, and 90minutes after the block and 1, 2, 4, 8, 12& 24hours after the end of surgery.

Sensory block for each dermatomes was assessed by a pinprick test using a 3-point scale:

- Score 0 =normal sensation.
- Score 1 =Absence of sensation of pinprick (analgesia).
- Score 2 = Absence of sensation of touch (anaesthesia)

Onset of sensory block time was defined as the time period between the end of the local anaesthetic administration to loss of touch sensation (score 2) in each dermatomes.

Duration of sensory block is defined as the time period between the ends of local anaesthetic injection to complete recovery of anaesthesia on each dermatomes.

Duration of analgesia were calculated from the end of local anaesthetic injection to the first complaint of pain.

Visual Analog Scale (0 –10) was used for postoperative pain assessment Inj. diclofenac 75 mg i.m. was given when the Visual Analog Scale >4.

Following Complication of paravertebral block were observed in intraoperative and post operative period.

- Failure of block
- Hypotension(less than 20% of baseline MAP)

- Bradycardia (<55 bpm)
- Pneumothorax.
- Intrathecal injection, postdural puncture headache
- Horner's syndrome, ipsilateral or bilateral.
- Unilateral arm sensory block (involved to T1 component of brachial plexus).
- Hematoma.
- Pulmonary haemorrege
- Local anaesthetic toxicity.

STATISTICAL ANALYSIS

The observations recorded in each group were compared using statistical analysis. The raw data collected using the protocol was converted into grouped data . After the collection of data, mean and standard deviation was calculated for each variable in both the groups.

If the two means in two groups were found to be separated by more than twice of standard error(>2SE) then the two means were considered as highly significant ($p<0.05$).If the two means were found to be separated by more than thrice of standard error(>3SE),then the two means were considered as very highly significant($p<0.001$).

ANOVA, Student's paired t test were used when data was normally distributed. The software used for calculation of p value was Stata (Version 10).

OBSERVATION AND RESULTS

The study was conducted in Tirunelveli Medical College Hospital. After obtaining approval from the Hospital Ethical Committee, sixty patients were randomized into two groups. Group BC consisted of patients receiving

bupivacaine with clonidine in PVB while Group B consisted of patients receiving bupivacaine only .

Randomisation was done using sealed envelope technique .After the completion of study, both the groups were compared.

There were totall failure of block in 3 cases of which 2 in Group B and 1 in Group BC. They were excluded from the study. In both the groups complications were not observed.

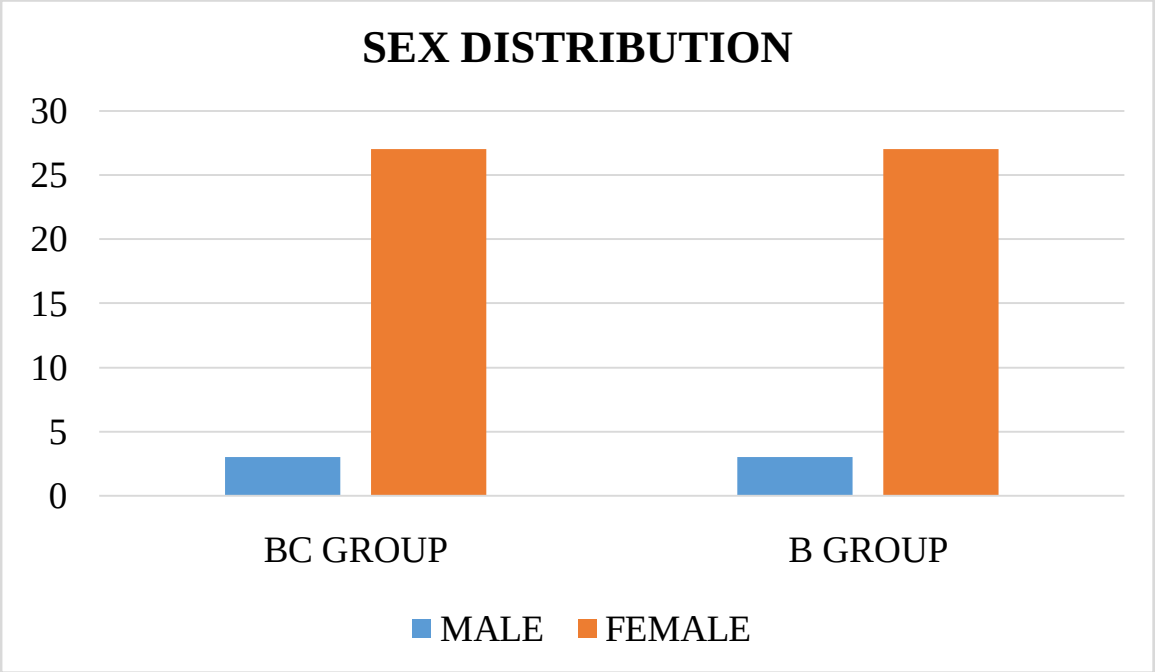
Age, weight of the patient and duration of surgery between both the groups were comparable and were not statistically significant (P>0.05)

TABLE - 6 SEX DISTRIBUTION

GROUP	SEX	FREQUENCY	PERCENT
BC GROUP	MALE	3	10.0
	FEMALE	27	90.0

B GROUP	**MALE**	3	10.0
	FEMALE	27	90.0

CHART-1COMPARISION OF SEX DISTRIBUTION BETWEEN THE TWO GROUPS



Comparison of sex distribution between the two groups is statistically not significant

Table – 7 Comparison of Age (yrs),Wt(kg) Distribution between the two groups

PARAMETER	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't'

					TEST
AGE	**BC**	30	32.90	11.260	0.832
	B	30	32.23	12.950	
WEIGHT	**BC**	30	55.33	6.445	0.759
	B	30	55.87	6.922	

CHART – 2 Comparison of Age (yrs) Distribution between the two groups

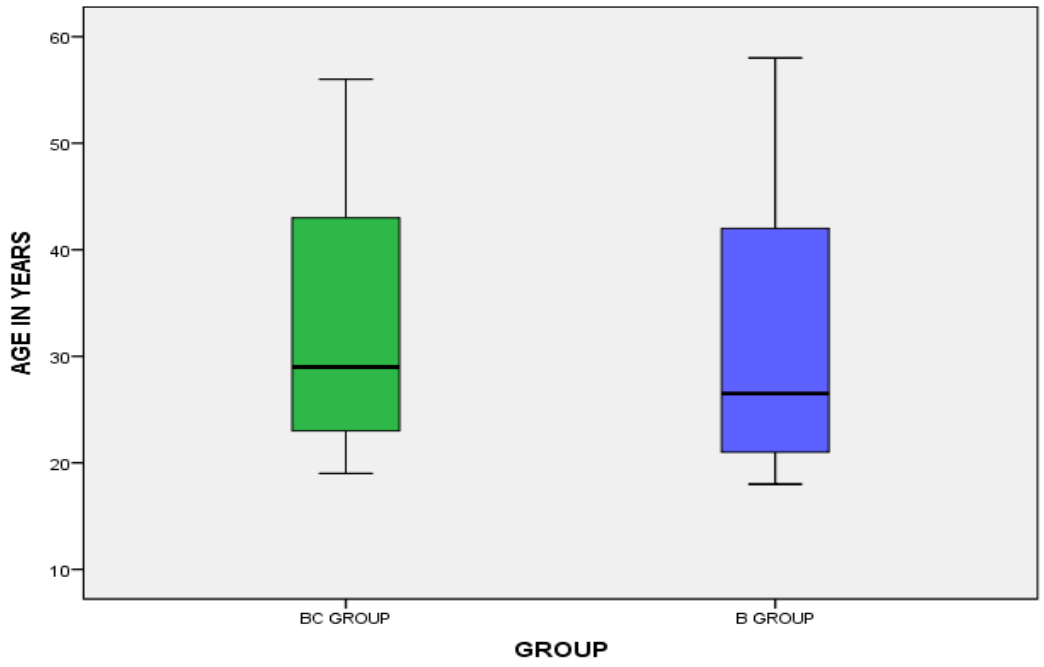
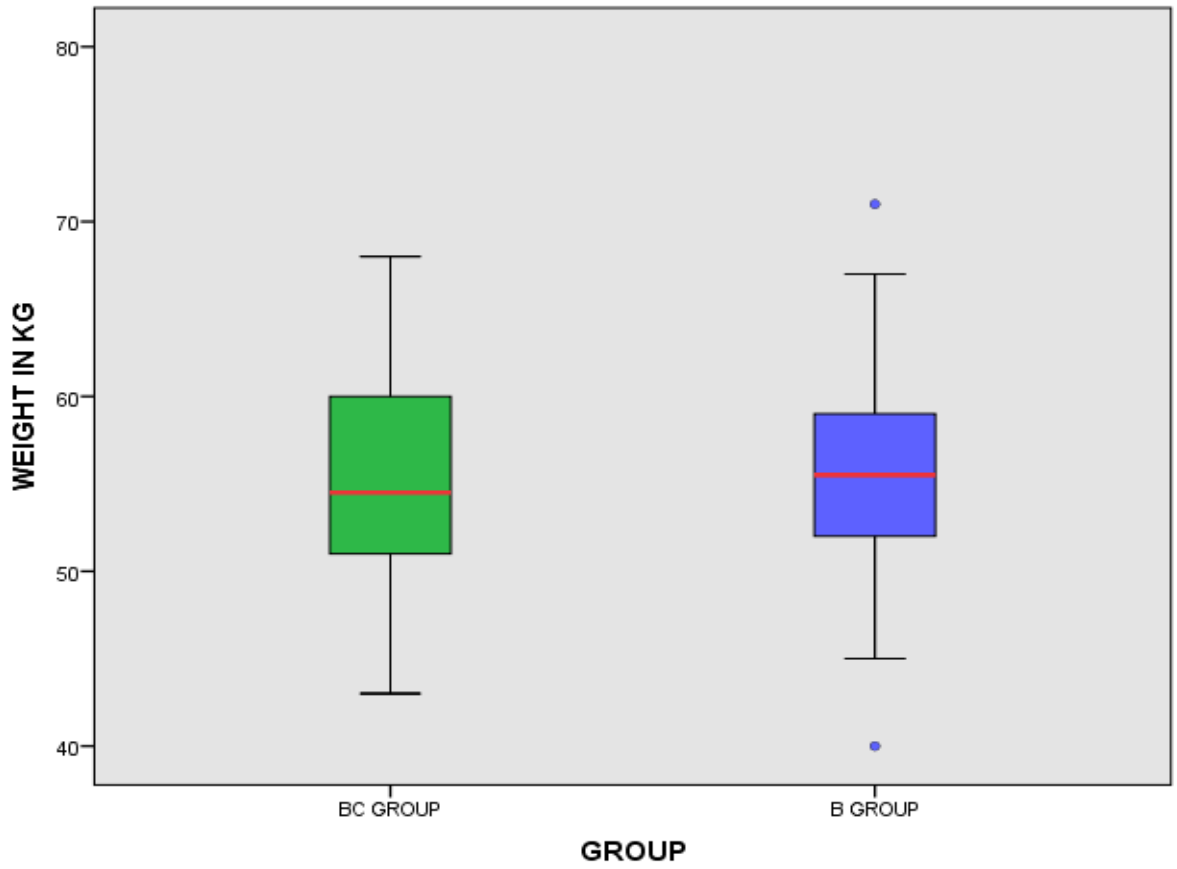


CHART – 3 Comparison of Wt(kg) Distribution between the two groups

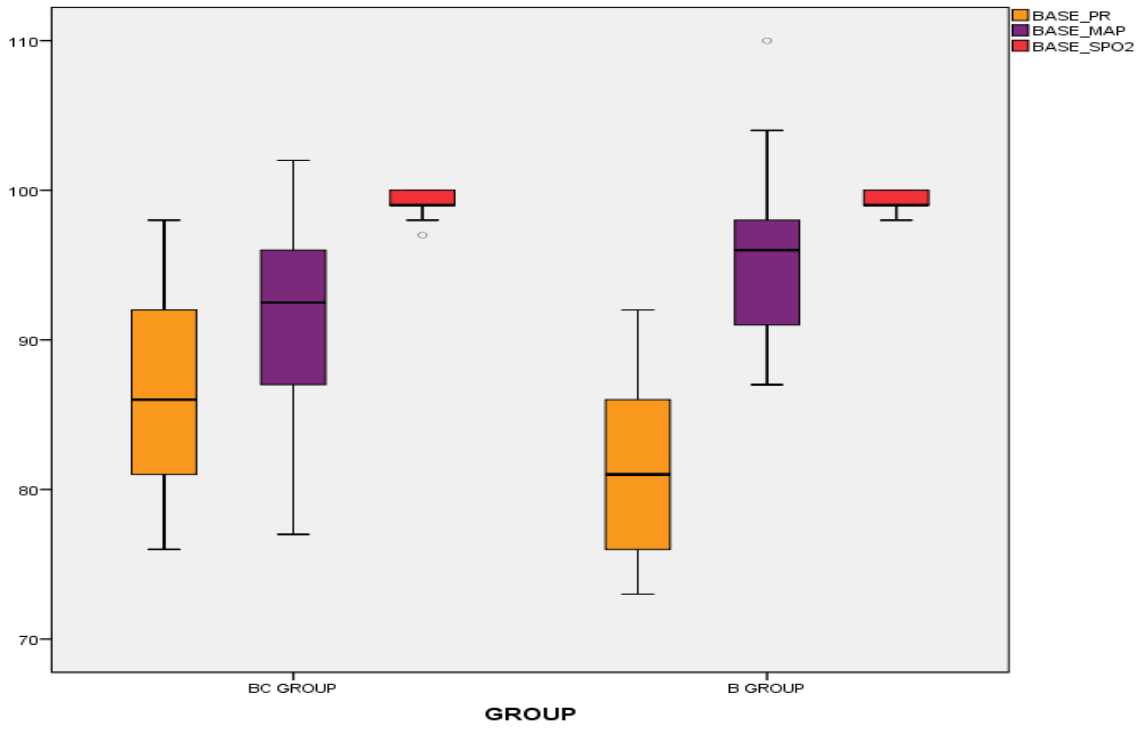


The mean age(yrs) and weight in kg of BC group was 32.9&55.33 and the B group was 32.33&55.87,the difference between two groups statiscally not significant (p>0.05).

Table-8 COMPARISON OF BASELINE PR, MAP,SPO2 BETWEEN THE TWO GROUPS

BASELINE PARAMETERS	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
PULSE RATE	BC	30	83.267	0.3308	0.15
	B	30	83.133	0.3039	
MEAN ARTERIAL PRESSURE	BC	30	91.467	5.1214	0.19
	B	30	91.533	5.4007	
SPO2	BC	30	99.067	0.7849	0.93
	B	30	99.367	0.5561	

CHART - 4 Comparison of baseline parameters between the two groups

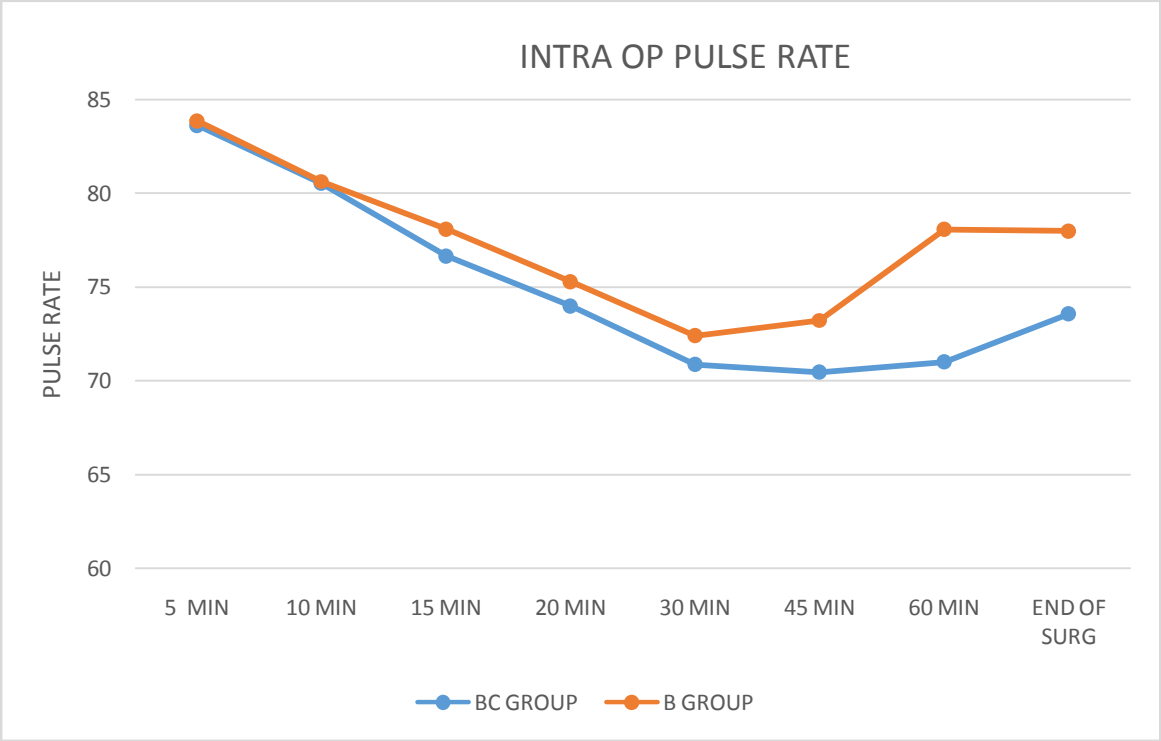


The preoperative baseline PR ,MAP,SPO2 among the two groups comparison were statistically not significant(p>0.05).

Table - 9 Comparison of intra operative PR between two groups at various intervels.

INTRA OP PULSE RATE	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
5 MIN	**BC**	30	83.367	5.4803	.562
	B	30	84.167	5.1333	
10 MIN	**BC**	30	80.167	4.6984	.493
	B	30	81.000	4.6535	
15 MIN	**BC**	30	75.867	4.5541	.012
	B	30	78.700	3.8430	
20 MIN	**BC**	29	72.90	3.876	.005
	B	30	75.80	3.727	
30 MIN	**BC**	29	69.93	3.380	.001
	B	30	72.80	2.999	
45 MIN	**BC**	12	68.92	2.234	.000
	B	14	73.79	2.607	
60 MIN	**BC**	5	70.40	2.702	.003
	B	3	80.00	3.000	
END OF SURGERY	**BC**	30	72.167	2.6920	0.001
	B	30	78.400	5.3019	

CHART – 5 Comparison of intra operative PR between two groups at various intervels

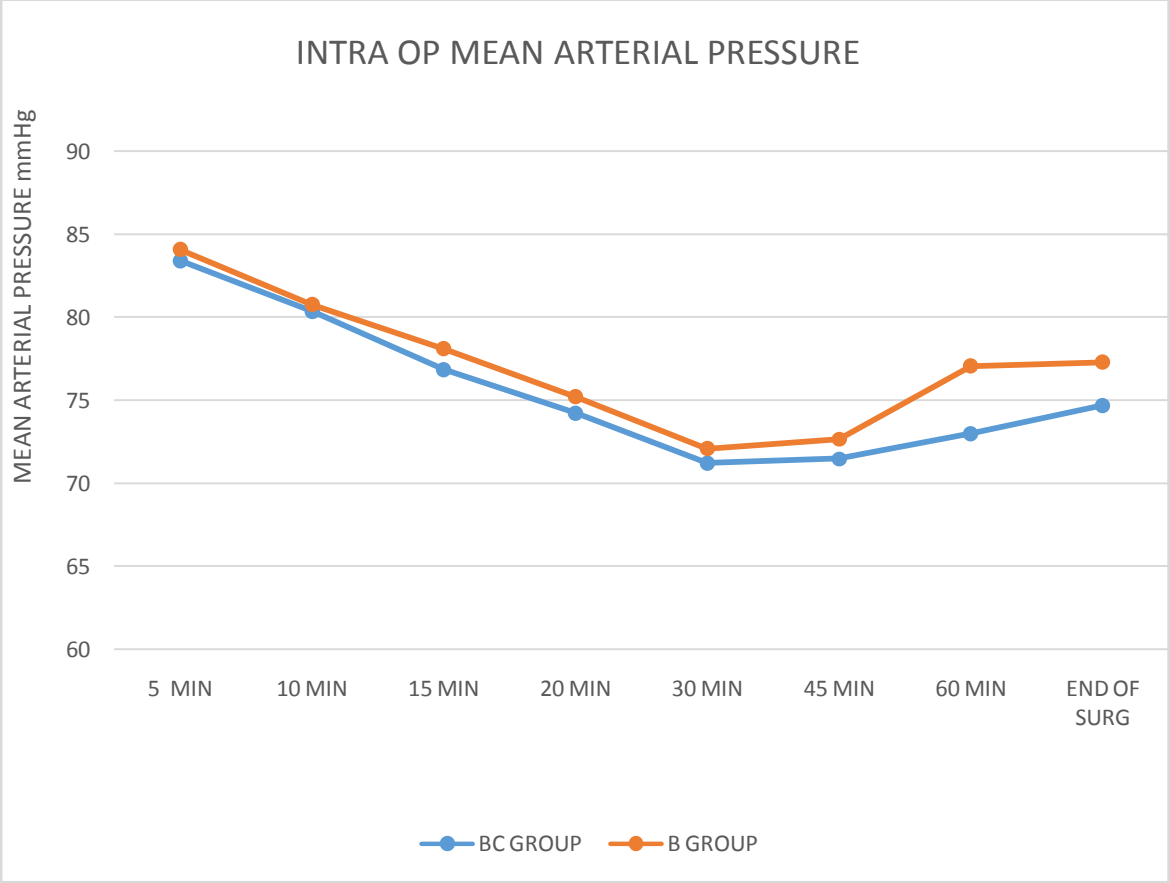


The mean intra operative PR was,lower in group BC ,Except 5th and 10thminute,when compared to group B.This was statistically significant($p<0.05$)

Table - 10 Comparison between two groups, intra operative MAP at various intervels

INTRA OP MEAN ARTERIAL PRESSURE	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
5 MIN	BC	30	93.700	3.7614	0.269
	B	30	92.367	5.3465	
10 MIN	BC	30	91.533	7.2194	0.911
	B	30	91.700	3.8070	
15 MIN	BC	30	86.700	4.4810	0.027
	B	30	89.033	3.3986	
20 MIN	BC	30	78.633	5.8338	0.001
	B	30	86.333	2.6436	
30 MIN	BC	30	75.433	5.3991	0.001
	B	30	81.600	2.7241	
45 MIN	BC	15	77.67	5.589	0.329
	B	14	79.21	2.045	
60 MIN	BC	5	80.80	5.070	0.802
	B	3	81.67	3.215	
END OF SURGERY	BC	30	85.967	6.7949	0.002
	B	30	81.167	3.9487	

CHART – 6 Comparison of intra operative MAP between two groups at various intervals

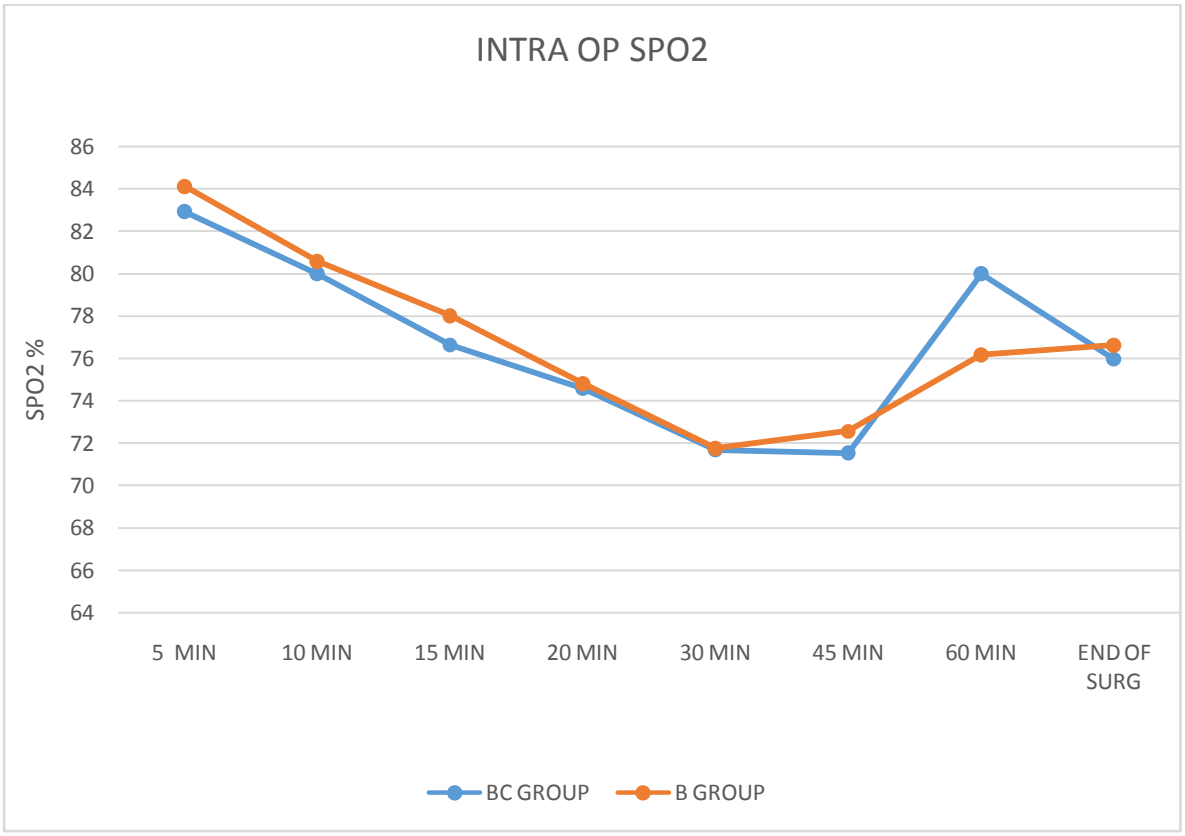


The mean intra operative MAP was lower in group BC, Except 5th and 10thminute,when compared to group B.This was statistically significant($p<0.05$). In 45th and 60th minutes p value is not significant,because frequency is small in both groups.

Table - 11 Comparison of intra operative SPO2 between two groups at regular intervals

INTRA OP SPO2	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
5 MIN	BC	30	98.600	.6747	0.155
	B	30	98.333	.7581	
10 MIN	BC	30	98.533	.5713	0.140
	B	30	98.233	.9353	
15 MIN	BC	30	98.300	.9523	0.354
	B	30	98.500	.6823	
20 MIN	BC	30	98.333	.7581	0.390
	B	30	98.500	.7311	
30 MIN	BC	30	98.867	.8193	0.253
	B	30	98.667	.4795	
45 MIN	BC	12	98.67	.492	0.320
	B	13	98.85	.376	
60 MIN	BC	5	98.80	.447	0.725
	B	3	98.67	.577	
END OF SURGERY	BC	30	98.533	.6814	0.385
	B	30	98.667	.4795	

CHART - 7 Comparison of intra operative SPO2 between two groups at regular intervals

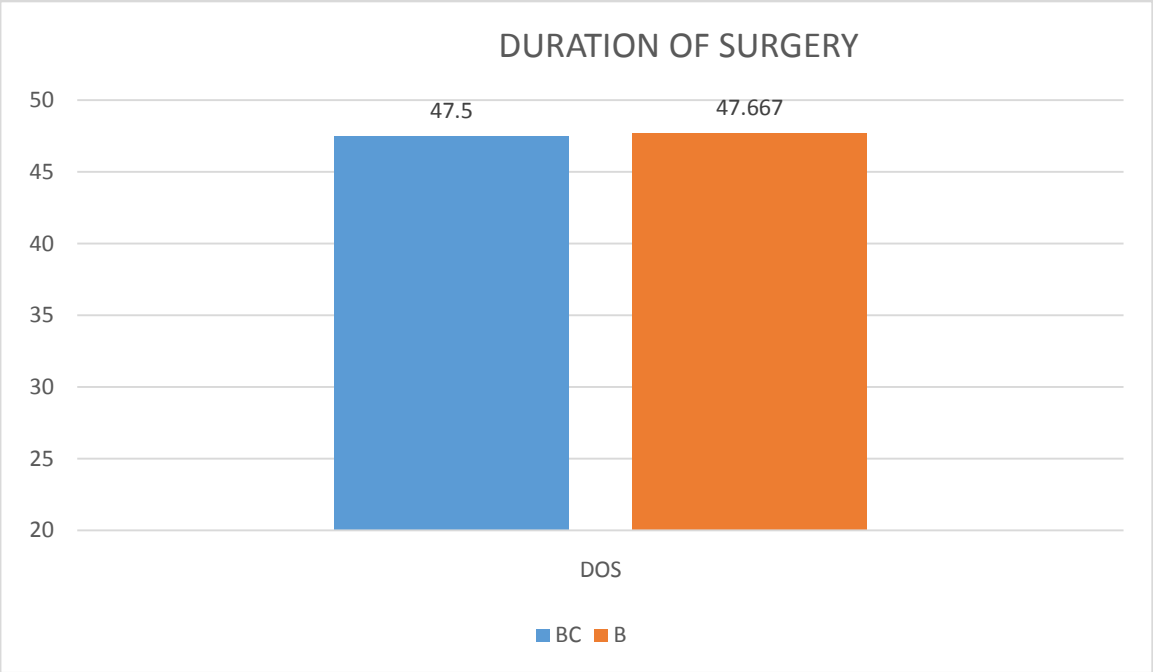


The mean intraoperative spo2 is equal in both groups,statistically not significant ($p>0.05$)

Table – 12 Comparison of duration of surgery between two groups

PARAMETER	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
DURATION OF SURGERY	BC	30	47.500	16.1218	0.933
	B	30	47.667	14.1259	

CHART-8 Comparison of duration of surgery between two groups

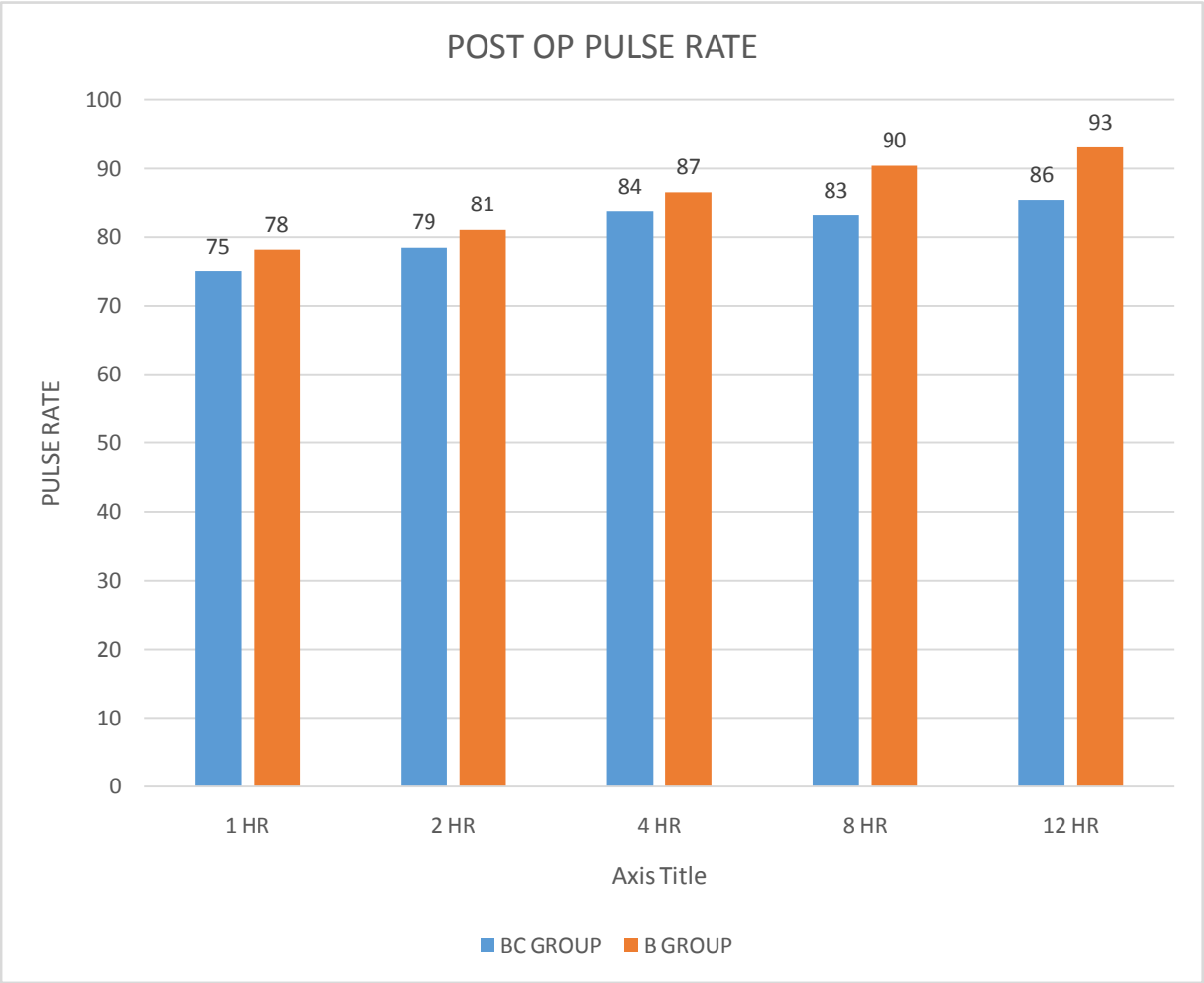


The mean duration of surgery in group BC was 47.5 minutes and group B was 47.667,difference between both the groups was statistically not significant(p>0.05).

Table - 13 Comparison of post operative PR between two groups at various intervals

POST OP PULSE RATE	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
1 HOUR	BC	30	74.400	4.9102	0.002
	B	30	78.633	4.9792	
2 HOUR	BC	30	77.967	4.3824	0.002
	B	30	81.533	3.9977	
4 HOUR	BC	30	82.733	4.6382	0.001
	B	30	87.000	3.5428	
8 HOUR	BC	30	80.833	5.1668	0.001
	B	30	91.400	3.5487	
12 HOUR	BC	30	83.500	4.7325	0.001
	B	30	93.667	4.0372	

CHART -9 Comparison of post operative PR between two groups at various intervals

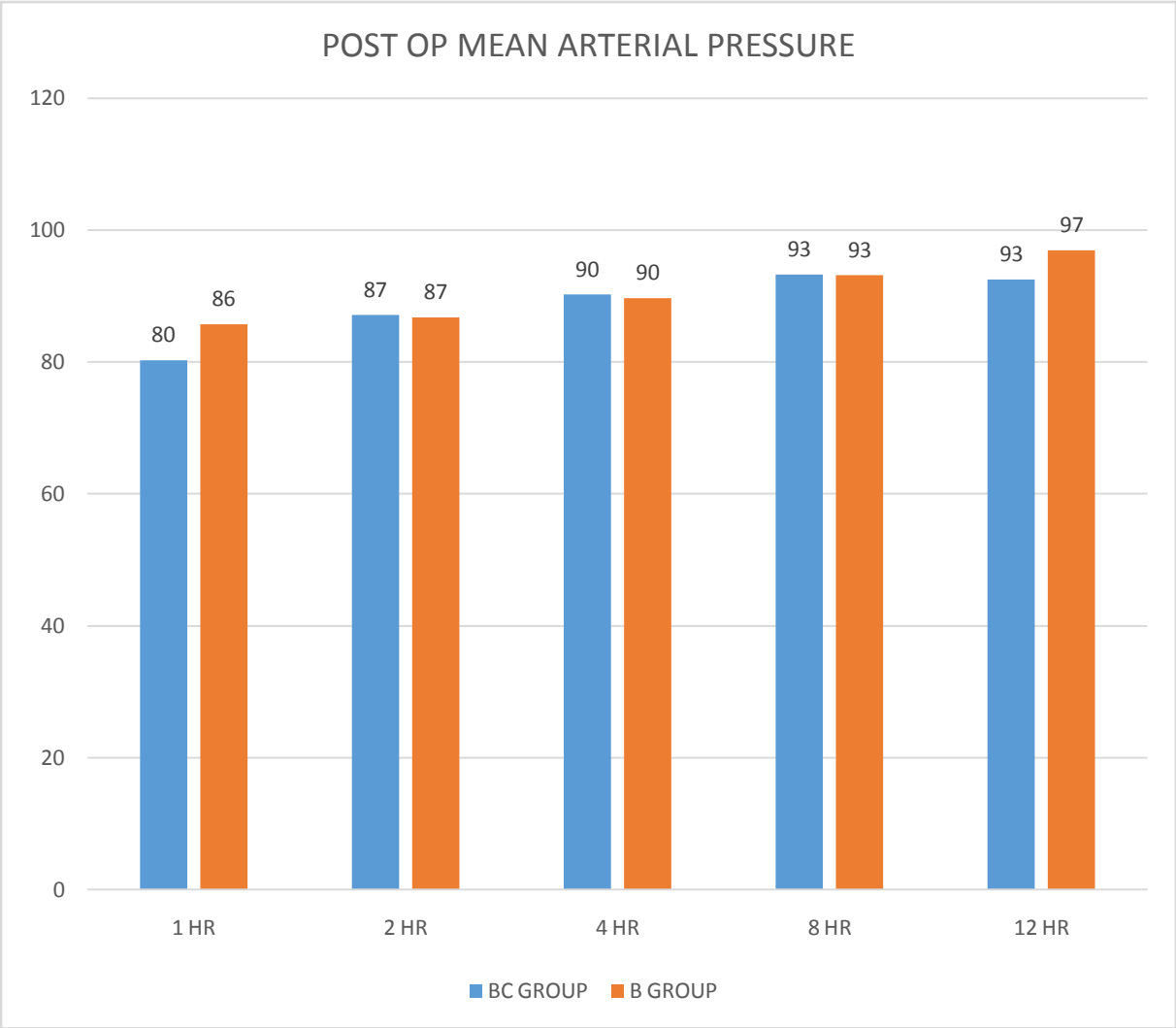


The mean postoperative PR was,lower in group BC ,when compared to group B. This was statistically significant($p<0.05$).

Table - 14 Comparison of post operative MAP between two groups at various intervals

POST OP MEAN ARTERIAL PRESSURE	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
1 HOUR	BC	30	78.633	5.8338	0.001
	B	30	86.533	2.5289	
2 HOUR	BC	30	86.933	4.5177	0.791
	B	30	87.200	3.1006	
4 HOUR	BC	30	89.400	5.1769	0.719
	B	30	89.800	3.1666	
8 HOUR	BC	30	92.667	4.3098	0.495
	B	30	93.300	2.6412	
12 HOUR	BC	30	91.867	5.8706	0.001
	B	30	97.233	2.6611	

CHART -10 Comparison of post operativeMAP between two groups at various intervals

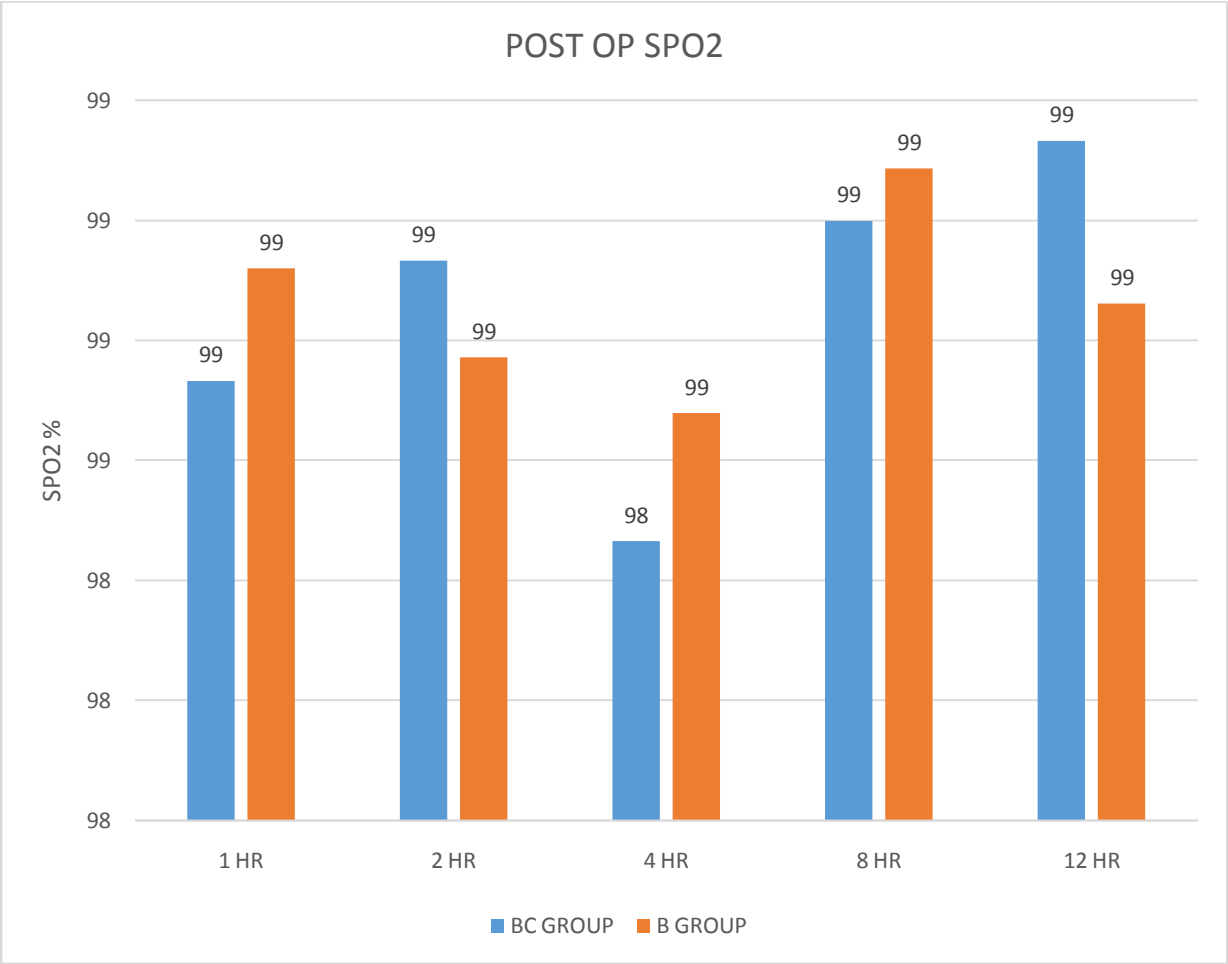


The mean of post operative MAP was low at 1HR and 12HR ,in group BC. It was statistically significant , when compared with group B.

Table:15 Comparison of post operative SPO2 between two groups at various intervals

POST OP SPO2	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
1 HOUR	BC	30	98.567	.6789	0.849
	B	30	98.600	.6747	
2 HOUR	BC	30	98.600	.5632	0.827
	B	30	98.633	.6149	
4 HOUR	BC	30	98.467	.8193	0.609
	B	30	98.567	.6789	
8 HOUR	BC	30	98.600	.7240	0.395
	B	30	98.733	.4498	
12 HOUR	BC	30	98.767	.4302	0.303
	B	30	98.633	.5561	

CHART11 Comparison of post operative SPO2 between two groups at various intervals

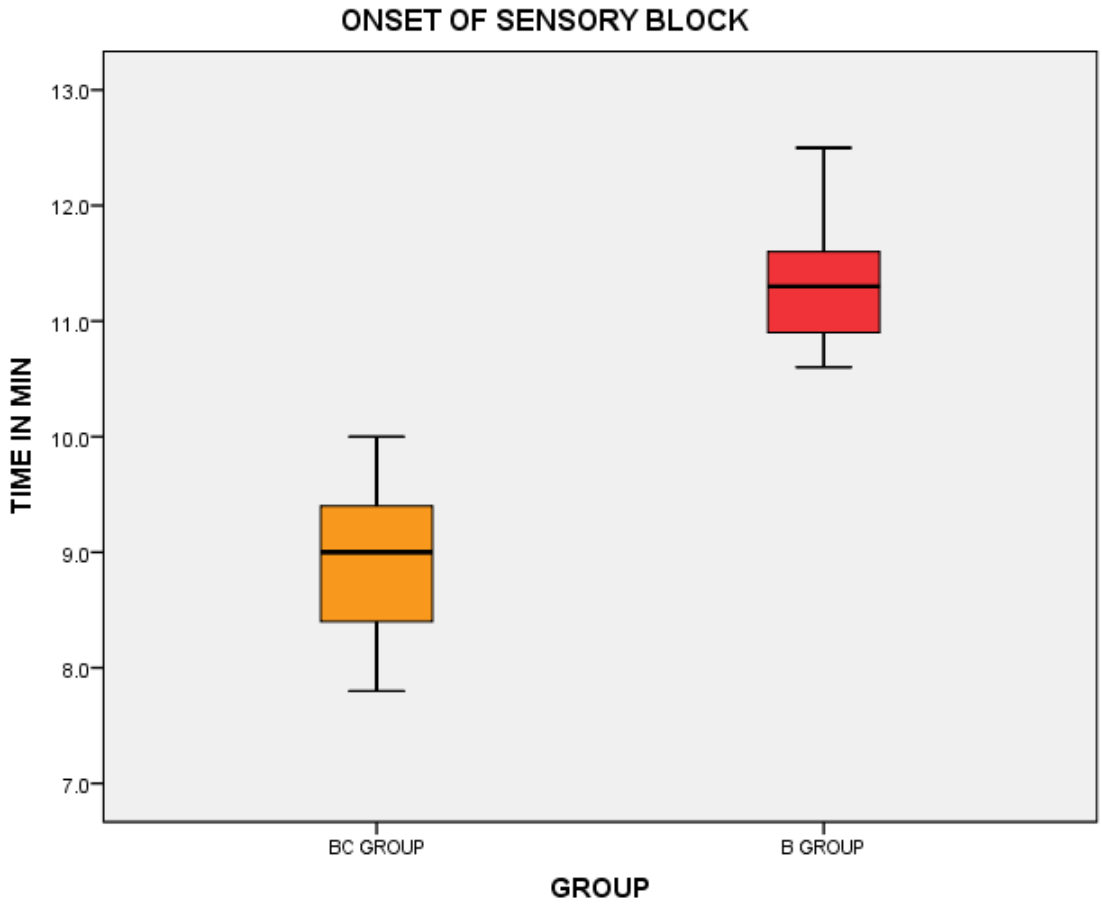


The mean postoperative spo2 is equal in both groups,statistically not significant (p>0.05).

Table - 16 Comparison of ONSET OF SENSORY block between two groups

PARAMETERS	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
ONSET OF SENSORY BLOCK	BC	30	8.937	.6403	0.001
	B	30	11.320	.4888	

CHART - 12 Comparison of ONSET OF SENSORY block between two groups

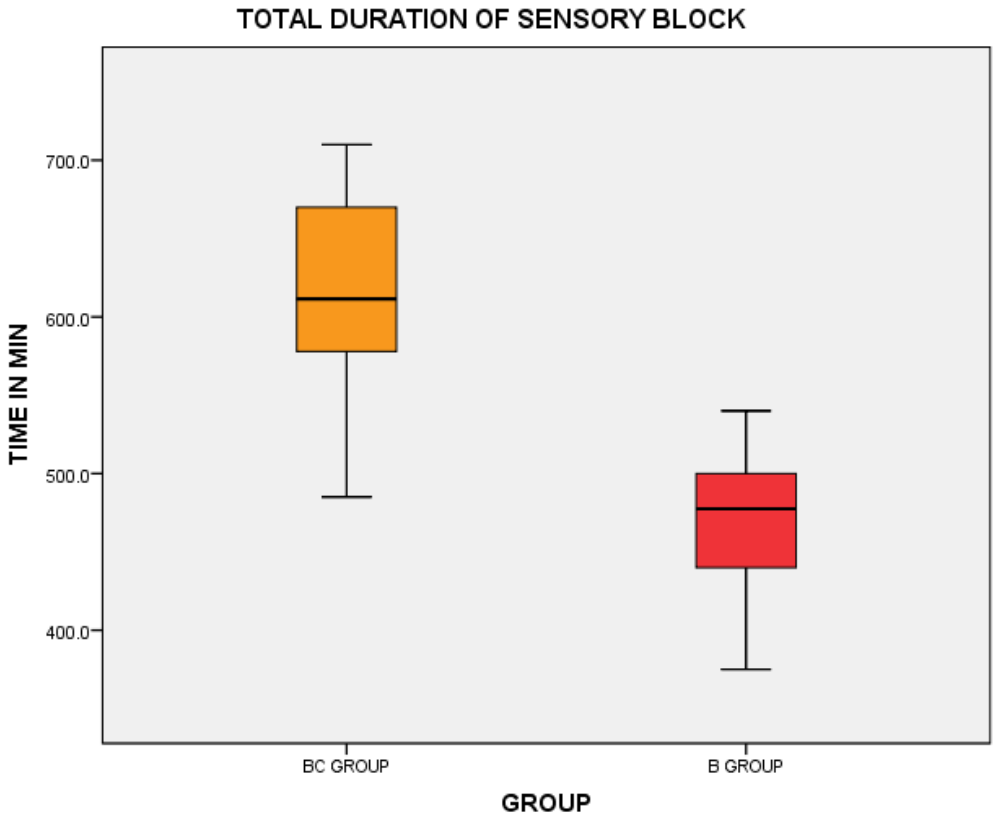


The mean onset of sensory block was 8.937 minutes in group BC and 11.32 minutes in group B .When compared it was statistically high significant($p<0.05$).

Table - 17 Comparison of total duration OF SENSORY block between two groups

PARAMETERS	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
TOTAL DURATION SENSORY BLOCK	**BC**	30	616.867	64.2515	0.001
	B	**30**	**465.167**	**48.0209**	

CHART - 13 Comparison of total duration OF SENSORY block between two groups

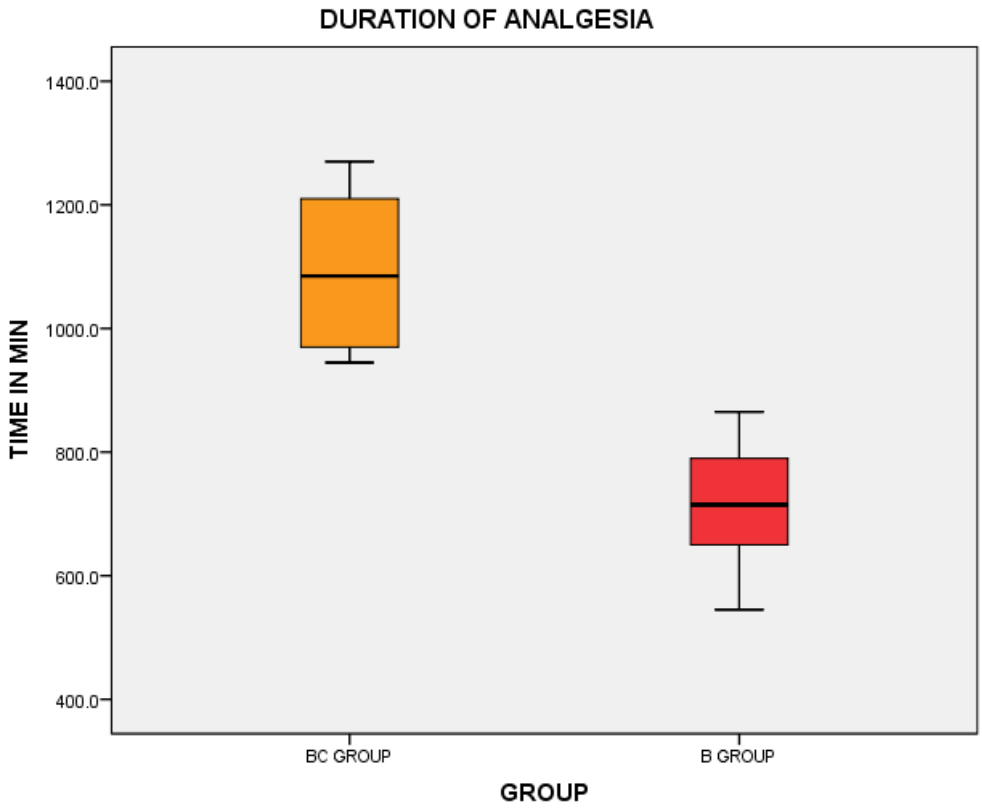


The mean total duration of sensory block was HIGH in group BC, when compared with group B. Its statistically highly significant($p<0.01$).

Table - 18 Comparison of duration of analgesia between two groups

PARAMETERS	GROUP	FREQUENCY	MEAN	STANDARD DEVIATION	p VALUE 't' TEST
DURATION OF ANALGESIA	BC	30	1098.000	117.3236	0.001
	B	30	713.000	86.5388	

CHART - 14 Comparison of duration of analgesia between two groups at various intervals.

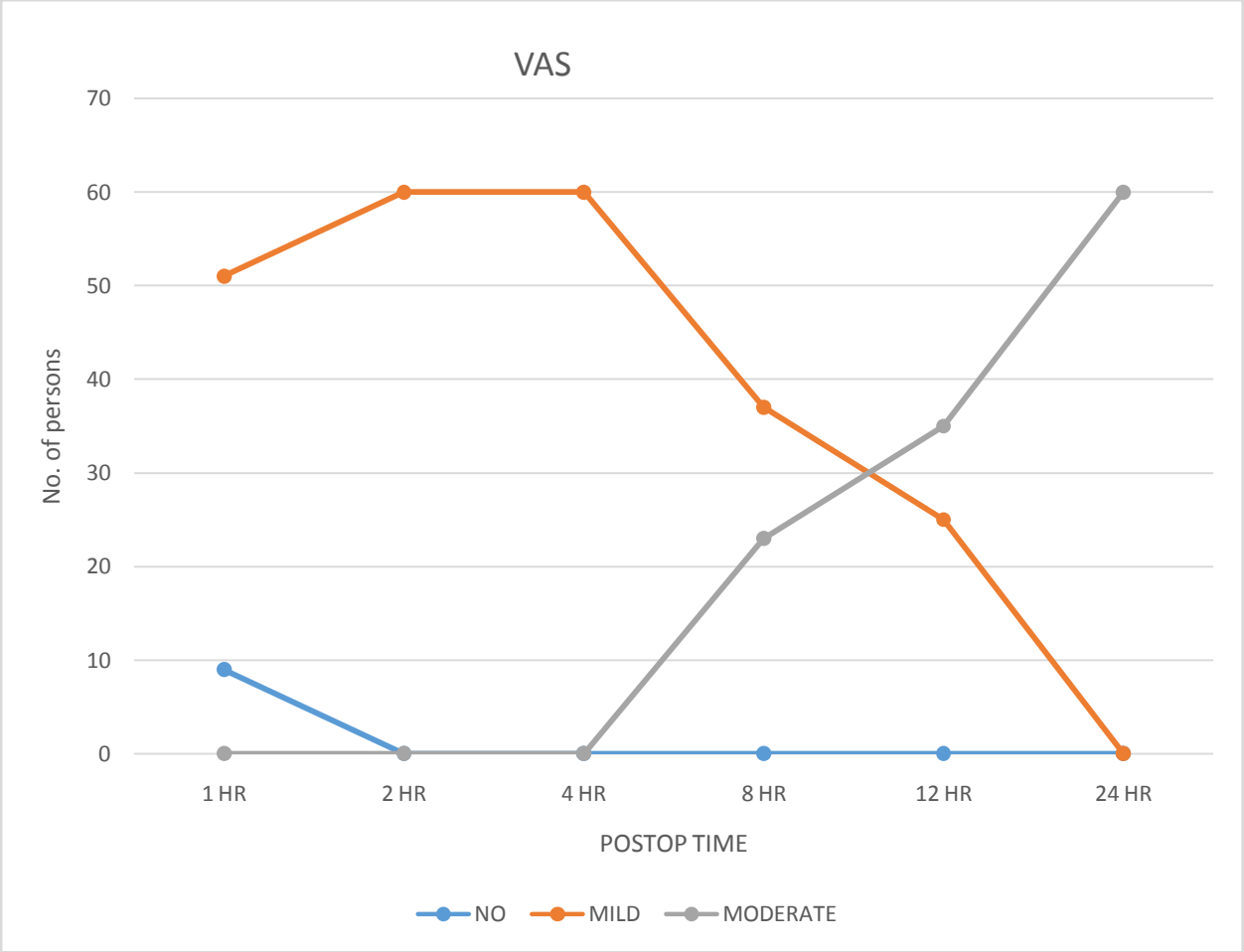


The mean duration of analgesia was 1098 minutes in group BC, and 713 minutes in group B when compared, It was statistically highly significant($p<0.05$).

Table - 19 Comparison of VISUAL ANALOG SCORE for pain between two groups a various intervals

VAS	GROUP	FREQUENCY	MEAN RANK	SUM OF RANKS	MANN WHITNEY U TEST	p VALUE 't' TEST
1 HOUR	**BC**	30	27.00	810.00	345.0	0.12
	B	30	34.00	1020.00		
2 HOUR	**BC**	30	19.00	570.00	105.0	0.001
	B	30	42.00	1260.00		
4 HOUR	**BC**	30	16.55	496.50	31.5	0.001
	B	30	44.45	1333.50		
8 HOUR	**BC**	30	16.32	489.50	24.5	0.001
	B	30	44.68	1340.50		
12 HOUR	**BC**	30	16.08	482.50	17.5	0.001
	B	30	44.92	1347.50		
24 HOUR	**BC**	30	15.83	475.00	10.0	0.001
	B	30	45.17	1355.00		

CHART - 15 Comparison of VISUAL ANALOG SCORE for pain between two groups a various intervals



The mean of VISUAL ANALOG SCORE was 1hr,2hr,4hr,8hr,12hr,24hr was low in group BC,when compared with group B.Its statistically significant ($p<0.05$) ,except 1hr VAS is not statistically significant.

Table - 20 Complication of PVB

COMPLICATION	Group BC	Group B
Faliure of block	1	2
Bradycardia	-	-
Hypotension	-	-
Pneumothorax	-	-
Vascular injection	-	-
Intrathecal injection	-	-
-Local anaesthetic toxicity	-	-
Unilateral Horners syndrome	-	-

There was totally three cases of failed block ,in both the groups.

DISCUSSION

In our study we observed ,demographic datas like age (yrs),sex,weight in(kg), ASA grade are not statistically significant ,when compared in both groups.

Diagnosis, procedure such as lumpectomy, excision, wepsterprocedure,simplemastectomy,and duration of surgery are not statistically significant , when compared both the groups.

Addition of clonidine with bupivacaine in thoracic paravertebral block,provided effective surgical anaesthesia and reduced the onset of sensory blockade time.It prolonged the total duration of sensory blockade time and also prolonged total duration of analgesia, when compared to control group.

Patients had low postoperative VISUAL ANALOG SCORE in 2HR,4HR,8HR.12HR,24HR. Patients were haemodynamically stable in both intraoperative and postoperative period and there was no bradycardia.

The α 2 agonists dose dependently, enhance the potency and prolong the duration of local anaesthetic by combining with α 2 receptors at peripheral level. The other action include

Vasoconstriction around the site of injection. Thus the absorption of local anaesthetic drug will be delayed, resulting in a prolongation of the local anaesthetic effect.

Clonidine directly inhibits the peripheral nerve action.

Release of local enkephalin like substances.

A decrease in the release of local inflammatory mediators.

Increase in the release of anti inflammatory cytokines.

Clonidine and Dexmedetomidine are the currently used α 2 receptor agonists.

In my study mean duration of analgesia is prolonged >18.3 HRS in group BC, which is closely related to ,**Weltz et al52** Fifteen patients with breast malignancies, who underwent surgical management under PVB, in the form of MRM with axillay dissection were studied retrospectively. The onset of sensory blockade was prolonged upto 23 hrs effectively relieving post operative pain.

In study conducted by **EbrahimyM&Moradi AR** , in patients posted for simple mastectomy ,PVB with bupivacaine was used. Duration of analgesia was 17hrs and all patients observed no pain for the first 8hrs after surgery, which was comparable to my study.

C. L. Burlacu ,H. P. Frizelle et al, studyobserved that, PVB with fentanyl and clonidine in combination with levobupivacaine (0.05%) are effective

analgesics, a significant reduced the supplemental postoperative morphine consumption after breast surgery.

In another study, HuraG,Knapik p et al,seventy patients receiving 0.5%ropivacaine and 0.5% bupivacaine inPVB for MRM, the onset of sensory blockade and duration of sensory blockade was analysed.both the group similar level of analgsia was achived. Results shows that.

GROUP	ONSET OF SENSORY BLOCKAE WITH IN 5 MIN	TOTAL DURATION OF SENSORY BLOCKADE > 24 HRS
R	53%	81%
B	20%	50%

In my study, the mean onset of sensory blockade time and total duration of sensory block in PVB,closely related to **Pusch F et al.**study ,single injection unilateral PVB at the level of T4 , using 0.5% bupivacaine,in breast surgery. It produced faster onset and prolonged duration of sensory block (3 hr to 10 hr),and high post operative pain score. It reduced the need for post operative analgesic doses.

Coveney et al - a retrospective study of 145 cases, who underwent surgical treatment for breast malignancies using paravertebral block and 100 cases receiving general anaesthesia alone. TPVB alone was enough for completing

the surgery in 85% of patients, while 5.7% of patients required supplementation with local anaesthetic.

In a study conducted by **Greengrass et al** ,twenty five patients underwent breast surgery with paravertebral block and sedation as an alternative to general anaesthesia .Postoperatively , patients had minimal nausea , vomiting and pain. The procedure was satisfactory for all patients.

In a study conducted by **Pekka et al** ,TPVB with 0.5% bupivacaine at the level T3,prior to general anaesthesia in patients posted for breast canser surgery(MRM).only three patients had pain on the first postoperative day in comparison to the control group which had twelve patients with postoperative pain(p=0.007).In the 24 hour postoperative followup, VAS scores were higher in the control group in comparison to the group receiving PVB block.

Klein et al , in their study of sixty patients,

found that patients receiving PVB experienced statistically significant less pain at 30 min, 1 hr, 24 hr and 72 hr in comparison to patients receiving GA only.

In our study, no complication occurred in both groups,except for 3 patients with failure of blockade, similar to study conducted by Moller and Greengrass.

Various studies on paravertebral blocks have quoted different rates of

complications.**Terheggen** reported one case with epidural block and one patient with pleural puncture.

Pekka has reported a single incidence of accidental intravascular injection of bupivacaine. **Coveney** has reported complication rate of 2.6% with two cases experiencing epidural extension while one patient developed pneumothorax.

CONCLUSION

The addition of clonidine (2 mics/kg) to 0.5% bupivacaine in thoracic paravertebral block for simple breast surgery produced, faster onset of sensory blockade.Its also prolonged the total duration of sensory block and duration of analgesia. It provided effective intraoperative and postoperative haemodynamic stability.

From our study we concluded that

1. Paravertebral block when used in alone provides effective surgical anaesthesia andsuperior analgesia in post operative period.

2. Paravertebral block reduces incidence of postoperative nausea and vomiting

3. Paravertebral block provided effective intraoperative and postoperative haemodynamic stability.

4. Paravertebral block leads to reduced hospital stay and early discharge.

5. Complication rates of paravertebral block are significantly low thereby proving it to be a relatively safe procedure.

SUMMARY

In our study , 60 patients receiveing paravertebral block in breast surgery, were allocated into two groups ,group BC receiveing 0.5% bupivacaine with clonidine and group B 0.5% bupivacaine alone

The addition of clonidine (2 mics/kg) to 0.5% bupivacaine in thoracic paravertebral block for simple breast surgery produced , faster onset of sensory blockade.It also prolonged the total duration of sensory block and duration of analgesia. It provided effective intraoperative and postoperative haemodynamic stability.

The procedure also proved to be safe as no complication was observed in patients, who received paravertebral block.

So PVB was easy to learn , safe to perform and patient friendly.

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ANNEXURE – I

CONSENT

Informed written consent.

Name of the patient- I.P. no-

I ,---------- in my full sense give my wholehearted consent for the surgery under axillary brachial plexus block with levobupivacaine and dexmedetomidine for study purpose. I agree that no responsibility will be attached to the surgeon or anaesthetist. I have been explained about the procedure in my own language.

Signature of the patient / guardian

PROFORMA

Case NO- I.P-no-

NAME AND ADDRESS OF THE PATIENT

Age- : Sex D.O.ADMISSION

History in brief-

Clinical diagnosis/ indication.

Examination in brief-

A. Vitals

a. Pulse b .B.P C**.** AIRWAY-ASSESSMENT

B. Systemic examination

Baseline haemodynamics :

PR: BP: SPO2:

INVESTIGATIONS

Hb% BT CT Blood urea Serum creatinine

RBS

Urine examination- Albumin Sugar Microscopy

Chest X-ray ECG ASA Grading-

Surgical procedure - **Duration-**

PARAMETERS OBSERVED-

- onset time for sensory block -
- Total duration of sensory block -
- Duration of analgesia –

Intra operative Monitoring:

Time after block	Heart rate	MAP	SPO2
5 min			
10 min			
15 min			
20 min			
30 min			
45 min			
60 min			
90 min			
EOS			

Postoperative Monitoring:

Time after surgery	Hearte rate	MAP	SPO2	VAS
1HR				
2HR				
4HR				
8HR				
12 HR				
24 HR				

S.NO	AGE	SEX	WT	DIAGNOSIS	S_X	BASELINE			INTRA OP PR								INRAOP MAP							
						PR	MAP	SPO_2	5M	10M	15M	20M	30M	45M	60M	EOS	5M	10M	15M	20M	30M	45M	60M	EOS
1	20	F	51	FA(LT)	Excision	84	91	99	88	84	76	69	67	-	-	72	93	86	84	77	79	-	-	82
2	22	F	48	FA(LT)	Excision	79	95	100	85	80	76	72	69	-	-	68	96	88	81	73	64	-	-	78
3	56	F	52	CA rt breast	SM	90	102	97	91	88	84	76	70	67	70	74	97	93	87	88	76	73	82	98
4	43	F	55	Phylloids tumor(rt)	SM	90	97	98	81	78	76	73	70	68	69	73	98	101	97	90	84	82	77	97
5	26	F	53	FA(RT)	E	76	83	99	75	73	71	68	69	-	-	68	89	101	87	76	69	-	-	82
6	35	F	56	FA(RT)	E	81	90	99	77	74	70	67	64	69	-	71	91	84	88	76	78	72	-	85
7	20	F	49	FA(RT)	E	87	89	98	92	86	80	76	73	-	-	76	96	87	84	79	77	-	-	89
8	19	F	45	FA(RT)	E	84	96	99	87	85	79	77	75	-	-	71	93	103	91	72	81	-	-	87
9	45	F	58	CA rt breast	SM	92	99	100	81	80	77	76	74	69	67	74	87	82	84	76	72	78	88	101
10	46	F	64	Phylloids tumor(lt)	SM	89	90	100	91	87	84	81	77	74	72	76	97	88	84	76	74	85	82	89
11	36	F	60	FA(RT)	E	86	87	99	88	84	80	77	74	-	-	70	89	88	84	76	76	-	--	84
12	55	F	51	Phylloids tumor(rt)	SM	90	97	99	96	88	86	80	75S	70	74	76	97	96	87	82	77	79	75	87
13	29	F	54	FA(LT)	E	78	92	98	81	78	74	69	67	-	-	73	91	84	88	76	78	-	-	76
14	30	F	57	FA(LT)	E	81	95	99	79	81	77	72	68	-	-	69	96	88	81	73	64	-	-	78
15	29	F	58	FA(LT)	E	84	86	100	82	80	74	68	66	-	-	72	97	93	87	88	76	-	-	77
16	29	F	63	FA(RT)	E	79	84	99	90	84	79	78	74	-	-	70	98	101	97	90	84	-	-	92
17	29	F	65	Lump rt breast	L	86	89	98	82	78	76	74	70	67	-	71	89	101	87	76	69	82	-	93
18	47	F	48	FA(RT)	E	82	93	99	78	75	71	68	64	-	-	74	96	88	81	73	64	-	-	89
19	26	F	54	FA(RT)	E	89	96	99	84	80	77	73	71	-	-	68	97	93	87	88	76	-	-	78
20	22	M	68	Gynecomastia(lt)	WP	78	97	99	80	77	75	72	69	66	-	74	98	101	97	90	84	82	-	86
21	48	M	66	Gynecomastia(rt)	WP	88	95	100	77	73	66	69	70	68	-	71	96	87	84	79	77	64	-	77
22	23	F	45	Lump rt breast	L	94	88	100	83	82	75	73	68	69	-	74	93	103	91	72	77	75	--	79
23	25	F	54	Lump lt breast	L	90	82	99	89	87	82	78	76	72	-	78	87	82	81	76	72	78	-	82
24	43	M	54	Gynecomastia(rt)	WP	88	85	98	78	76	72	70	68	-	-	70	97	88	84	76	74	85	-	84
25	32	F	59	FA(RT)	Excision	90	86	99	86	79	75	73	70	-	-	76	89	88	84	76	76	73	-	78
26	29	F	61	Lump rt breast	L	87	87	99	74	71	69	64	66	68	-	70	97	96	87	82	77	79	-	89
27	19	F	43	FA(RT)	E	78	96	99	81	77	73	70	71	-	-	69	91	84	88	76	78	-	-	90
28	23	F	52	FA(LT)	E	82	99	100	85	82	74	72	69	-	-	73	96	87	84	79	77	-	-	87
29	31	F	56	FA(LT)	E	85	101	100	80	81	75	74	72	-	-	71	93	103	91	72	81	-	-	93
30	50	F	61	FA(LT)	E	88	77	100	80	77	73	69	67	-	-	73	87	82	84	76	72	78	-	92

INTRA OP SPO_2								DOS	POST OP PR					POST OP MAP					POST OP SPO_2					VAS						OSB MIN	TDSB MN	DOA
5 M	10 M	15 M	20 M	30M	45 M	60 M	EO S		1H	2H	4H	8H	12H	1H	2H	4H	8H	12H	1H	2H	4H	8H	12 H	1H	2H	4H	8H	12H	24 H			
99	98	99	98	99	-	-	99	35	68	78	80	77	88	77	84	86	87	91	98	99	99	97	99	0	1	1	2	3	4	7.9	665	1145
98	99	99	98	99	-	-	97	40	74	79	88	84	85	73	81	85	89	95	97	98	99	99	98	1	1	1	2	3	4	8.7	605	1210
99	97	98	99	97	98	99	99	75	81	84	85	91	91	88	87	84	95	102	99	99	98	97	98	1	1	2	3	4	5	9.8	543	965
97	98	99	98	99	99	98	99	80	83	78	86	89	81	90	97	93	97	101	98	99	99	99	99	1	1	2	3	4	5	9.7	485	945
99	98	99	99	97	-	-	98	35	75	77	81	78	75	76	87	78	83	83	99	98	99	98	99	0	1	1	2	3	4	8.6	670	1085
99	99	98	99	99	99	-	98	55	78	83	75	73	85	76	88	87	89	90	99	98	99	99	99	1	1	1	2	3	4	7.8	710	970
99	98	99	98	99	-	-	99	40	76	86	77	76	83	79	84	91	95	89	98	99	97	99	98	1	1	1	2	3	4	9	698	1025
98	99	99	97	98	-	-	99	35	80	78	92	86	87	72	91	95	99	96	99	97	99	99	99	0	1	1	2	3	4	10	705	1155
97	98	99	98	100	99	99	99	75	73	75	87	85	81	76	84	92	93	103	99	99	98	99	99	1	1	2	3	3	4	8.5	495	965
99	99	99	99	99	98	99	98	85	69	78	81	86	91	76	84	88	87	90	99	99	99	97	98	1	1	2	3	4	5	8.4	590	970
99	99	98	98	99	-	-	99	35	72	79	84	87	88	76	84	89	97	87	99	98	99	99	99	1	1	1	2	3	4	8.2	610	1265
99	99	97	99	100	99	99	99	80	78	71	81	84	92	82	87	83	89	97	97	99	99	99	99	1	1	2	2	3	4	9	578	1020
99	98	99	97	99	-	-	97	35	79	76	96	88	81	76	88	85	97	92	99	99	98	99	99	1	1	1	2	3	4	8	705	1215
99	99	98	99	99	-	-	99	40	69	78	81	78	79	73	81	87	91	95	99	98	97	99	99	1	1	1	2	3	4	8.1	550	1265
98	99	96	97	99	-	-	98	40	74	83	79	81	82	88	87	93	96	86	99	99	99	98	99	0	1	1	3	4	5	8.7	567	1135
99	98	97	99	99	-	-	99	35	68	75	82	80	90	90	97	99	97	84	99	99	97	99	99	1	1	1	2	3	4	8.5	613	1200
99	99	98	99	100	99	-	99	50	75	77	85	84	82	76	87	96	98	89	97	99	96	99	98	1	1	2	2	3	4	8.3	497	1025
99	99	98	99	97	-	--	98	40	79	78	82	78	78	73	81	93	89	93	99	98	99	99	99	1	1	1	2	3	4	9.3	570	1270
99	98	99	99	99	-	-	97	35	69	85	78	75	84	88	87	95	96	96	99	99	98	97	99	1	1	1	2	3	4	9.4	625	1085
98	99	99	99	99	99	-	99	50	78	83	84	80	85	90	97	97	97	97	98	99	98	99	99	1	1	2	3	4	5	9.1	610	970
99	99	97	98	99	99	-	99	55	71	77	80	77	84	79	84	89	90	95	99	99	99	98	99	1	1	1	2	3	4	9.2	595	1010
99	98	99	97	99	98	-	98	55	83	78	77	73	83	72	91	86	93	88	99	98	99	99	99	1	1	1	2	3	4	9.4	620	945
97	99	98	99	100	99	-	99	50	81	75	83	82	89	76	81	88	96	82	99	99	98	99	99	1	1	2	2	3	4	9	595	970
99	99	96	99	98	-	-	99	30	73	69	89	87	78	76	84	89	87	85	98	99	98	99	98	0	1	1	2	3	4	10	610	1140
99	99	99	98	99	-	-	98	40	70	73	78	76	86	76	84	87	97	86	99	98	99	99	99	1	1	1	2	3	4	9.5	710	1270
99	98	99	97	99	98		99	55	79	74	86	79	74	82	87	90	89	89	98	99	99	99	99	0	1	2	3	3	4	9.6	685	980
98	99	97	99	100	-	-	99	35	69	72	79	71	81	76	88	79	87	102	99	99	99	98	99	0	1	1	2	3	4	9.7	645	1265
98	99	99	98	99	-	-	99	40	68	75	81	77	85	79	84	87	91	92	99	98	99	99	99	1	1	1	2	3	4	9.4	625	1150
99	98	99	99	98	-	-	98	35	72	87	85	82	78	72	91	95	96	95	98	99	99	99	98	0	1	1	2	3	4	8.4	655	1245
99	98	99	98	99	-	-	99	35	68	78	80	81	79	76	91	96	93	86	99	98	99	99	99	1	1	1	2	3	4	8.9	675	1080

S.NO	AGE	SEX	WT	DIAGNOSIS	S_X	BASELINE			INTRA OP PR								INTRA OP MAP							
						PR	MAP	SPO	5 M	10M	15M	20M	30M	45M	60M	EOS	5M	10 M	15 M	20 M	30M	45 M	60 M	EOS
1	24	F	52	FA(RT)	Excision	88	93	99	84	**80**	**78**	**73**	72	-	-	**78**	**102**	95	93	88	84	-	-	82
2	20	M	48	Gynecomastia(rt)	WP	85	96	100	91	**87**	**85**	**83**	78	75	-	**79**	**95**	97	96	93	87	80	-	78
3	42	F	61	Lump breast (rt)	L	76	88	100	90	**88**	**87**	**85**	81	77	-	**84**	**99**	93	89	86	80	77	-	80
4	18	F	40	FA(RT)	E	81	89	100	86	**84**	**81**	**77**	73	-	-	**78**	**90**	89	87	85	76	-	-	77
5	40	F	56	Lump breast(rt)	L	82	89	99	77	**75**	**76**	**72**	68	72	-	**78**	**89**	95	93	90	82	78	-	76
6	40	F	58	Lump breast(lt)	L	84	91	99	85	**82**	**79**	**79**	75	74	-	**83**	**96**	99	91	89	86	82	-	80
7	19	F	54	FA(RT)	E	92	90	98	88	**82**	**77**	**74**	76	-	-	**79**	**103**	93	90	87	83	-	-	81
8	18	F	45	FA(RT)	E	87	93	99	78	**74**	**76**	**73**	71	-	-	**78**	**90**	87	89	86	80	-	-	78
9	45	F	66	FA(LT)	E	81	87	100	79	**81**	**79**	**76**	74	77	-	**85**	**87**	86	81	82	78	76	-	82
10	25	F	67	FA(RT)	E	86	97	100	85	**81**	**76**	**76**	73	-	-	**78**	**97**	96	87	85	80	-	-	78
11	21	F	50	FA(RT)	E	88	89	99	84	**80**	**82**	**78**	75	-	-	**79**	**92**	90	89	87	82	-	-	80
12	20	F	55	FA(LT)	E	82	92	99	92	**87**	**84**	**81**	76	-	-	**71**	**95**	91	89	86	81	-	-	77
13	56	F	52	Ca breast(rt)	SM	91	94	99	88	**85**	**80**	**77**	73	75	80	**93**	**86**	89	85	82	77	81	84	93
14	18	F	59	FA(RT)	E	79	96	99	**75**	**78**	**74**	**72**	69	-	-	**78**	**84**	85	87	84	79	-	-	77
15	48	M	71	Gynecomastia(lt)	WP	82	92	100	**79**	**77**	**73**	**74**	72	70	-	**76**	**89**	87	84	85	80	77	--	78
16	26	M	64	Gynecomastia(lt)	WP	90	91	100	**95**	**89**	**84**	**81**	75	74	-	**75**	**93**	89	90	89	84	80	-	82
17	24	F	54	FA(RT)	E	82	89	99	**87**	**85**	**80**	**79**	73	--	-	**77**	**96**	92	89	87	82	-	-	80
18	58	F	59	Ca breast (lt)	SM	78	96	99	**81**	**74**	**72**	**69**	71	76	83	**92**	**97**	97	90	87	85	82	78	85
19	18	F	46	FA(RT)	E	87	92	100	**84**	**79**	**75**	**73**	70	-	-	**77**	**95**	90	87	85	80	-	-	78
20	24	F	55	FA(LT)	E	76	90	99	**79**	**77**	**79**	**74**	71	-	-	**75**	**88**	93	87	85	81	-	-	86
21	52	F	58	Phylloids tumor(rt)	SM	87	95	99	**84**	**82**	**78**	**73**	71	73	77	**86**	**87**	90	85	82	80	78	83	90
22	38	F	59	Lump breast (rt)	L	83	93	100	**79**	**83**	**79**	**76**	74	76	-	**78**	**85**	87	93	87	84	82	-	86
23	35	F	62	Lump breast (lt)	L	78	87	99	**89**	**87**	**83**	**79**	78	74	-	**75**	**86**	97	90	89	82	78	--	81
24	36	F	64	FA(RT)	E	84	97	99	**78**	**77**	**76**	**74**	70	-	-	**69**	**89**	89	85	84	80	-	-	84
25	31	F	52	FA(LT)	E	86	89	100	**78**	**75**	**73**	**71**	72	-	-	**73**	**98**	87	89	85	81	-	-	85
26	45	F	56	Lump breast (lt)	L	74	90	99	**91**	**89**	**84**	**79**	70	68	-	**74**	**92**	91	89	87	84	80	-	78
27	54	F	55	Lump breast (rt)	L	85	91	99	**81**	**75**	**79**	**74**	69	72	-	**77**	**95**	96	91	87	82	78	-	81
28	23	F	48	FA(RT)	E	79	90	100	**85**	**77**	**75**	**72**	70	-	-	**75**	**88**	93	96	90	86	-	-	82
29	27	F	58	FA(LT)	E	81	93	100	**88**	82	**80**	**76**	73	-	-	**76**	**87**	95	93	89	84	-	-	80
30	22	F	52	FA(LT)	E	80	87	99	**85**	**78**	**77**	**74**	71	-	-	**76**	**101**	93	87	82	78	-	-	80

INTRA OP SPO_2								DOS	POST OP PR					POST OP MAP					POST OP SPO_2					VAS						OSB	TDSB	DOA
5M	10 M	15 M	20 M	30 M	45 M	60 M	EOS		1H	2H	4H	8H	12H	1H	2H	4H	8H	12 H	1H	2H	4H	8H	12 H	1H	2H	4H	8H	12H	24 H			
98	99	98	97	99	-	-	99	35	**78**	82	84	93	92	88	91	95	97	99	97	99	99	98	99	1	1	2	3	4	5	11.2	485	835
99	98	99	99	98	99	-	98	50	**77**	83	90	95	99	93	89	88	93	97	99	99	98	99	98	1	2	3	4	5	7	11	440	660
97	99	98	99	99	98	-	99	55	**84**	80	86	92	94	86	85	86	90	93	99	98	99	99	99	1	2	3	4	5	6	10.8	395	645
99	97	99	98	99	-	-	98	40	**78**	83	87	93	96	85	87	90	93	99	97	99	99	98	99	1	2	3	4	5	6	10.9	410	690
99	98	99	99	98	99	-	99	50	**78**	81	86	91	89	90	93	95	97	99	99	99	99	99	98	1	2	3	4	5	6	11.4	445	705
97	99	99	98	99	99	-	99	55	**83**	87	94	99	96	89	88	86	90	97	99	99	98	99	99	1	1	2	3	4	5	11.7	490	865
99	98	98	99	99	-	-	98	35	**79**	81	86	93	95	87	85	89	93	97	98	98	99	99	99	1	1	2	3	4	5	11.5	460	790
98	99	99	98	99	-	-	99	40	**78**	82	88	90	89	86	87	93	96	99	99	99	97	99	99	1	2	3	4	5	6	12	525	695
99	97	98	99	98	99	-	99	50	**85**	86	89	93	95	82	79	86	87	89	99	98	99	99	99	1	2	3	4	5	6	10.6	515	590
98	99	99	98	99	-	-	98	40	**78**	78	83	85	89	85	83	89	93	97	98	99	99	98	99	1	1	2	3	4	6	10.9	490	745
98	96	99	99	98	-	-	99	40	**79**	80	85	90	94	87	89	91	95	99	99	98	99	99	98	1	2	3	4	5	6	11	445	610
97	99	98	99	99	-	-	99	35	**71**	77	87	91	98	86	89	93	95	96	99	99	98	99	99	0	1	2	3	4	5	11-4	500	845
99	97	99	97	99	98	99	98	80	**89**	93	93	96	101	82	87	93	97	102	99	99	99	99	98	1	2	3	4	5	7	11.3	395	545
99	99	98	99	99	-	-	99	40	**78**	80	86	93	95	84	89	88	93	97	99	97	99	98	99	1	2	3	4	5	6	12	385	615
98	98	99	99	98	99	-	99	50	**76**	78	83	89	90	85	85	86	90	93	99	99	99	99	98	1	2	3	4	5	7	12.3	470	660
99	98	99	97	99	99	-	99	55	**75**	79	93	95	99	89	87	90	93	99	99	99	98	99	99	1	2	3	4	5	6	12.5	445	710
97	99	98	99	99	--	-	98	35	**77**	80	88	93	95	87	93	95	97	99	98	99	99	99	98	1	2	3	4	5	7	11.4	470	740
99	98	99	99	98	99	99	99	85	**92**	89	94	97	100	87	88	86	90	97	99	99	99	98	99	1	1	2	3	4	6	116	375	595
98	97	99	99	99	-	-	99	40	**77**	80	85	90	95	85	85	89	93	97	99	97	99	99	99	1	2	3	4	5	6	11	490	680
99	99	98	97	99	-	-	99	35	**75**	79	86	93	94	85	87	93	96	99	99	99	98	99	97	1	2	3	4	5	6	10.9	510	720
99	96	99	99	99	99	98	98	85	**86**	90	88	94	97	82	84	87	93	101	98	99	99	98	99	1	2	3	4	5	6	10.8	380	585
98	99	99	98	99	99	-	99	55	**78**	82	89	87	86	87	83	89	93	97	99	98	99	99	99	1	2	3	4	5	6	11.3	465	650
99	99	97	99	99		-	99	50	**75**	81	87	95	99	89	89	94	96	94	99	99	99	99	99	1	2	3	4	5	6	11.4	520	730
97	98	99	99	98	-	-	98	35	**70**	76	90	89	94	84	87	89	93	99	98	99	97	99	98	1	2	3	4	5	6	12	505	725
99	98	99	98	99	-	-	99	40	**73**	77	79	85	89	85	89	88	93	97	99	98	99	98	99	1	1	2	3	4	6	11.4	540	830
98	99	98	99	99	99	-	99	50	**74**	78	87	91	88	87	85	86	90	93	99	99	99	99	99	1	2	3	4	5	6	11.7	485	770
99	98	99	99	98	99	-	98	55	**77**	81	86	89	90	87	87	90	93	99	99	98	99	98	99	1	2	3	4	5	6	10.8	490	790
99	99	97	99	98	-	-	99	35	**75**	78	81	85	89	90	93	95	97	99	98	99	97	99	98	1	2	3	4	5	6	10.7	410	750
98	99	99	98	99	-	-	99	40	80	83	84	87	90	88	88	86	90	97	99	99	98	99	99	1	2	3	4	5	6	10.9	525	825
98	99	97	99	98	-	-	98	40	84	82	86	89	93	89	85	89	93	97	97	99	98	99	98	1	2	3	4	5	6	11.2	495	795